Original Research Article

Prediction of significant hyperbilirubinemia using first 24 hour serum bilirubin level in healthy term neonates

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ABSTRACT

Background: Hyperbilirubinemia is most common cause for readmission after early hospital discharge. Severe jaundice and even kernicterus can occur in full term healthy newborns discharged early with no apparent early findings of hemolysis. The objective of the study was to evaluate whether the first 24 hour total serum bilirubin (TSB) value can predict development of significant hyperbilirubinemia subsequently in healthy term neonates.

Methods: A prospective study was conducted at tertiary care centre in Rajasthan, India during period of October 2010 to September 2011. Healthy full term newborns (gestational age ≥ 37 weeks) without any significant illness and Rh hemolysis were included. Serum bilirubin was estimated in all included neonates within 18 to 30 (24 ± 6 hour) hour of life using Diazo method (absorbance at 552 nm). The neonates were followed up clinically using Kramer's rule (after first bilirubin estimation at 24 hours of age) every 12 hour till discharge and recalled at fifth day of life after discharge. TSB estimation was repeated on fifth day of life or early (if clinical assessment of jaundice >10 mg/dl before discharge of baby). Hyperbilirubinemia was defined as TSB level >12 mg/dl at 25 to 48 hour of life, >15 mg/dl between 49 to 72 hours, and >17 mg/dl beyond 72 hours of life.

Results: A total of 100 neonates were enrolled in the study. Of these, 12 neonates developed hyperbilirubinemia. The mean first 24 hour TSB value in the neonates who subsequently developed hyperbilirubinemia was 7.03 ± 1.10 mg/dl as compared to a value of 5.22 ± 1.61 mg/dl in those who did not develop hyperbilirubinemia subsequently. The difference was significant ($p < 0.001$). Using Receiver operating characteristic (ROC) curve analysis, a value of 6 mg/dl (first 24 hour TSB) was determined to have the best predictive ability for subsequent hyperbilirubinemia. A TSB level of < 6 mg/dl at 24 ± 6 hour was present in 65 neonates and only 2 neonates developed hyperbilirubinemia subsequently. In the remaining 35 neonates with TSB > 6 mg/dl, subsequent hyperbilirubinemia developed in 10. (Sensitivity 83.33%, specificity 71.59, positive predictive value 28.57%, negative predictive value 96.92%).

Conclusions: Estimation of first day TSB level can help in prediction of neonates who would and who would not develop subsequent hyperbilirubinemia. Neonates with the first day TSB level of less than 6 mg/dl have minimum risk of subsequent hyperbilirubinemia.

Keywords: Hyperbilirubinemia, Neonates, Serum bilirubin

INTRODUCTION

Hyperbilirubinemia is a cause of concern for the parents as well as pediatricians. It occurs in approximately 60% of term neonates and 80% of preterm neonates during

first week of life.¹ Majority of times it is a physiological event, but in several neonates pathological jaundice occurs. Significant hyperbilirubinemia occurs in 5-10% of healthy term infants and is most common reason for readmission after early hospital discharge.²⁻⁴ Severe

jaundice and even kernicterus can occur in some full term healthy newborns discharged early with no apparent early findings of hemolysis.⁵

American academy of pediatrics (AAP) recommends that newborns discharged within 48 hours should have a follow up visit after 2-3 days to detect significant jaundice and other problems.⁶ Implementation of this recommendation may not be possible in all cases in our country due to limited follow-up facilities and other reasons. Financial constraints, family and medical consideration, shortage of hospital beds and personnel, frequently influence the decision about early hospital discharge of the mother and infant after birth. So there is an obvious need to develop simple predictive guidelines that will enable the physicians to predict or to identify which of the early discharged newborns will develop significant hyperbilirubinemia, and thereby helping to prevent its ill effects.

The present study is designed to determine the value of first 24 hours (+6 hours) serum bilirubin level that will predict subsequent hyperbilirubinemia in healthy term newborns.

METHODS

This was a prospective study conducted at tertiary care centre in Rajasthan, India during period of October 2010 to September 2011, after obtaining permission from ethical committee of institute. Healthy term neonates born during this period were included in the study. Only full term babies (gestation age >37 weeks, determined by LMP and confirmed by new Ballard score) whose parents agreed to come for follow-up were included in study. Babies were enrolled in present study only after taking prior informed consent from parents. Babies with significant illness requiring NICU admission for >12 hour, major congenital malformations, Rh incompatibility, conjugated hyperbilirubinemia and those lost to follow-up before the completion of 5 days of life were excluded from the study. Hyperbilirubinemia was defined as total serum bilirubin level >12mg/dl at 25 to 48 hour of life, >15 mg/dl between 49 to 72 hours, and >17 mg/dl beyond 72 hours of life.

Serum bilirubin estimation was done initially at 24±6 hours of age using Diazo method (absorbance at 552 nm) and analysed by biochemistry auto analyzer. Repeat serum bilirubin estimation was performed on fifth day of life or early (if clinical assessment of jaundice >10 mg/dl before discharge of baby).

The neonates were followed up clinically using Kramer's rule (after first bilirubin estimation at 24 hours of age) every 12 hour till discharge for appearance and progression of jaundice.⁷ The neonates were recalled after discharge on fifth day of life or early if the parents found their baby significantly icteric for clinical assessment and rechecking of serum bilirubin.

Statistical analysis

The value of first day serum bilirubin which will predict, with reasonable accuracy, the neonates at risk of subsequent hyperbilirubinemia was determined using receiver operating characteristic (ROC) curve analysis. The sensitivity, specificity, positive and negative predictive values of the test was calculated.

RESULTS

A total of 100 healthy full term neonates whose complete information was available, were included in the study. Their baseline characteristics are shown in Table 1.

Table 1: Baseline characteristics of study group.

Characteristics		Number
Maternal		
Parity	1	52
	2	32
	≥3	16
Mode of delivery	Vaginal	74
	Cesarean	22
	Instrumental	4
Maternal age	≤25 years	62
	26-30 years	30
	>30 years	8
Blood group	A+	38
	B+	30
	AB+	10
	O+	22
Neonatal		
Male		57
Female		43
Gestational age		37.94 ± 0.75 weeks
Birth weight		2815 ± 250 grams
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Maternal		
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Male		57
Female		43
Gestational age		37.94±0.75 weeks
Birth weight		2815±250 grams

Mean TSB value at 24±6 hours of age was 5.44±1.66 mg/dl. At the end of study, 12 neonates developed significant hyperbilirubinemia and all of these required phototherapy and none required exchange transfusion.

Table 2: Difference in first day TSB levels between group 1 and 2.

Group	Mean TSB level (mg/dl) at 24±6 hour of life
Neonates who developed significant hyperbilirubinemia	7.03±1.10
Neonates who did not develop significant hyperbilirubinemia	5.22±1.61

P-value < 0.001

Table 3: Predictive value of 24±6 hour serum bilirubin level.

Total serum bilirubin (24±6 hour)	No. of neonates	Neonates with significant hyperbilirubinemia
< 6 mg/dl	65	2
≥ 6 mg/dl	35	10

Sensitivity: 83.33%; Specificity: 71.59; PPV: 28.57%; NPV: 96.92%.

Whole study population divided in two subgroups: group 1 - neonates who developed significant hyperbilirubinemia and group 2 - neonates who did not develop significant hyperbilirubinemia. The mean±SD TSB level in neonates who developed hyperbilirubinemia was 7.03±1.10 mg/dl as compared to 5.22±1.61 mg/dl in those who did not develop significant hyperbilirubinemia subsequently. The difference of TSB level at 24±6 hours of age between neonates who did and those who did not develop hyperbilirubinemia was highly significant. (P value < 0.001) (Table 2).

Receiver operating characteristic curve analysis was used to determine the cut-off value of first day serum bilirubin which would predict neonates likely to develop significant hyperbilirubinemia (Figure 1). The cut-off TSB level of 6 mg/dl had best combination of sensitivity and specificity and was determined to predict subsequent hyperbilirubinemia. TSB level of <6 mg/dl at 24±6 hours of age was present in 65 neonates and only two neonates developed significant hyperbilirubinemia subsequently. In remaining 35 neonates, with TSB level >6 mg/dl, subsequent hyperbilirubinemia developed in 10 neonates. At this level of first 24±6 hours serum bilirubin, there are various predictive parameters (Table 3). Babies with TSB level < 6 mg/dl at 24±6 hours of age had very minimal risk of developing significant hyperbilirubinemia subsequently and those with TSB >6 mg/dl had a significant risk of developing subsequent hyperbilirubinemia.

Figure 1: Receiver operating characteristic curve for identifying best cut-off for subsequent hyperbilirubinemia.

DISCUSSION

The present study hypothesis was that a high serum bilirubin level soon after birth (within 24±6 hour of life), would also predict a high peak subsequently. In present study significant difference was found in first 24 hour serum bilirubin level between neonates who developed and those who did not develop significant hyperbilirubinemia subsequently. The present study found that a TSB level of <6 mg/dl at 24±6 hour can be used to predict the decreased risk for subsequent hyperbilirubinemia, such infants could thus be discharged early without need to follow up for hyperbilirubinemia later.

Bhutani et al showed in a large cohort that infants who develop hyperbilirubinemia have serum bilirubin levels, which are in higher percentiles soon after birth. The authors created percentile charts of serum bilirubin level at different postnatal ages in near-term and term infants who were direct Coombs test negative. They found that 6.1% neonates had predischarge serum bilirubin in the ≥95th percentile range and 32.1% of these neonates subsequently developed significant hyperbilirubinemia. Neonates with pre-discharge TSB levels in the low risk zone (< 40th percentile) did not show hyperbilirubinemia subsequently.⁸

In a similar study by Alpay et al a first day serum bilirubin of 6mg/dl was determined to have the highest sensitivity (90%).⁹ This critical bilirubin level had a very high negative predictive value (97.9%) and a fairly low positive predictive value (26.2%).

Awasthi et al showed that TSB level of 3.99 mg/dl at 18-24 hour was able to predict subsequent hyperbilirubinemia (>15 mg/dl) with sensitivity and specificity of 67% each. However, this study had major flaws. Complete follow up was present in infants who stayed in the hospital either for neonatal illness or some maternal reason, such as cesarean section. More than

50% of infants, who were healthy thus discharged early, were not followed up.¹⁰

In a study by Agarwal et al, the predictive ability of TSB = 6 mg/dl at 24±6 hour of life was evaluated and a sensitivity of 95%, specificity of 27.2% and negative predictive value of 99.3% were determined.¹¹

Present study population was heterogeneous (Table 1). The incidence of hyperbilirubinemia was determined to be 12%. The study had a few limitations. The infants were evaluated clinically for progression of jaundice and clinical assessment might not be considered very accurate by some. The infants were followed up to the 5th day of life and it is possible that some of these babies might have developed late jaundice and were missed.

CONCLUSION

The present study proves that a first day TSB of less than 6 mg/dl predicts the low risk of subsequent hyperbilirubinemia with high probability and these neonates can be discharged early from the hospital. Prediction of neonatal hyperbilirubinemia should have widespread implication especially in our country where there are limited resources and few hospital beds.

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REFERENCES

1. Behrman RE, Kliegman RM, Stanton BF, Schor NF. Jaundice and hyperbilirubinemia in newborn. In: Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders, 2012: 605-12.
2. Narang A, Gathwala G, Kumar P. Neonatal Jaundice: An analysis of 551 cases. Indian Pediatr. 1997;34:429-32.
3. Singhal PK, Singh M, Paul VK, Deorari AK, Ghorpade MG. Spectrum of neonatal hyperbilirubinemia: an analysis of 454 cases. Indian Pediatr. 1992;29:319-25.
4. Brown AK, Johnson L. Loss of concern about jaundice and the reemergence of kernicterus in the era of managed care. In: Fanroff AA, Klaus MH, Eds. The Year Book of Neonatal and Perinatal Medicine. Philadelphia; Mosby. 1996:17-28.
5. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term neonates. Pediatrics. 1995;96:730-3.
6. American academy of pediatrics. Practice parameter: Management of hyper-bilirubinemia in the healthy term newborn. Pediatrics. 1994;94:558-67.
7. Kramer LI. Advancement of dermal icterus in the jaundiced newborn. Amer J Dis Child. 1969;118:454-8.
8. Bhutani VK, Johnson L, Sivieri EM. Predictive ability of a predischage hour - specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near term newborns. Pediatrics. 1999;103:6-14.
9. Alpay F, Sarici SU, Tosuncuk HD, Serdar MA, Inanc N, Gokcay E. The value of first day bilirubin measurement in predicting the development of significant hyperbilirubinemia in healthy term newborns. Pediatrics. 2000;106:16.
10. Awasthi S, Rehman H. Early prediction of neonatal hyperbilirubinemia. Indian J Pediatr. 1998;65:131-9.
11. Agarwal R, Kaushal M, Agarwal R, Paul VK, Deorari AK. Early neonatal hyperbilirubinemia using first day serum bilirubin level. Indian Pediatrics. 2002;39:724-30.

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