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RESEARCH ARTICLE

UMBILICAL CORD BLOOD BILIRUBIN AS A PREDICTOR FOR NEONATAL HYPERBILIRUBINEMIA

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ABSTRACT

Jaundice is a clinical condition that is often present in pediatric practice and constitutes one of the major issues within the neonatal period. It occurs in both the physiological and pathological processes in newborns. The present study was conducted to verify whether the bilirubin levels found in the cord blood at birth could be indicative of neonatal hyperbilirubinemia among healthy term neonates. 567 term neonates were included in the study and subjected to a cord blood analysis for serum bilirubin. Further at 72 hrs of life, blood for serum bilirubin was again collected and the two values compared. With Receiver operating characteristic analysis, a cutoff value of cord bilirubin level of ≥1.89mg/dL was determined which had the highest sensitivity (96.36%) to predict the newborns who would develop significant hyperbilirubinemia. In present study, the cord bilirubin level of >1.89 mg/dL had the highest sensitivity (96.36%), and this critical bilirubin level had a very high (99.45%) negative predictive value and fairly low (26.4%) positive predictive value this finding compatible with other studies. The cord bilirubin level of <1.89 mg/dL did not completely exclude the development of significant hyperbilirubinemia; only 0.546% of the newborns with cord bilirubin levels of <1.89mg/dL developed jaundice. A 99.45% negative predictive value in the present study suggests that measurement of cord serum bilirubin can help in identify those newborns who are unlikely to require further evaluation and intervention. Estimating cord bilirubin levels is a simple and non invasive screening test to predict those neonates who are at least risk of developing significant hyperbilirubinemia and unlikely to require further evaluation and intervention.

Key words: Neonatal jaundice, hyperbilirubinemia, Cord bilirubin, phototherapy

INTRODUCTION:

Jaundice is a clinical condition that is often present in pediatric practice and constitutes one of the major issues within the neonatal period. It occurs in both the physiological and pathological processes in newborns. Each year, approximately 60% of the 4 million newborns in the United States are believed to become clinically jaundiced [1]. Such data is not available for India. When the newborn stays at the hospital for a 72-hour post-delivery period, it is possible to observe the peaking of the physiological jaundice, thus allowing medical intervention, if necessary.

However, in cases of early discharge from the hospital, the newborn may be subject to readmission for phototherapy treatment, because of high levels of unconjugated bilirubin which is the most common cause of readmission to NICU in early neonatal period. Such readmission, besides involving extra expenses for both the family and the institution, also exposes a probably healthy newborn to the hospital environment, brings emotional problems and risks to breast-feeding, and is one of the causes of early weaning [2]. The recognition, follow-up, and early treatment of jaundice has become more difficult as a result of earlier discharge from the hospital. Severe jaundice, and even kernicterus, can occur in some full-term healthy newborns discharged early with no apparent early findings of hemolysis [3,4].

The American Academy of pediatrics recommends that newborn discharged within 48hours should have a follow up visit after 2-3 days for any significant jaundice and other problems. 5 This recommendation is not appropriate for our country due to limited follow up facilities. Therefore , it is difficult to predict which infants are at increased risk for significant and relatively late hyperbilirubinemia. The present study was conducted to evaluate the predictive value of cord bilirubin level for identifying term infants at risk for subsequent hyperbilirubinemia.

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MATERIAL AND METHODS

The present study was conducted in a tertiary care hospital in South India from October 2010 to September 2011. Term baby with birth weight ≥ 2500gms were included in the study. Newborn babies with ABO / Rh incompatability, sick babies and babies born to mothers with significant illness were excluded from this study.

At the time of birth Cord bilirubin, Blood grouping, Cord heamatocrit estimation was performed. The cord bilirubin value was unknown to the member of the departmental staff who observed the neonates. The cord serum bilirubin was measured using a bichromatic (540, 700) endpoint technique. TBI Flex reagent cartridge,Cat.No.DF167 used. After the birth, the neonates were carefully followed up clinically with special emphasis on the appearance of jaundice.

After 72 hrs, serum bilirubin was estimated for all the neonates in the hospital who were included in the study group and those neonates who were discharged within 72hrs were advised to come on 4th day for re estimation of serum bilirubin. Umbilical cord blood serum bilirubin levels of the neonates were compared with those estimated after 72 hours. Neonates with serum bilirubin levels of ≥17 mg/dL after 72 hours of life were defined as having Significant hyperbilirubinemia [1,4].

In all cases, gender, birth weight, gestational age, delivery route, feeding pattern, Apgar scores, whether the mother had acquired any chronic diseases (hypertension, diabetes mellitus, etc) during gestation and mother's blood group were recorded. Informed consent was obtained from all parents of the new-borns enrolled in the study.

Statistical data were analyzed with the independent sample t test and the descriptive analysis and $\chi 2$ tests. The critical cord bilirubin level having the highest sensitivity was determined with the receiver operating characteristic (ROC) curve analysis. Sensitivity, specificity, negative and positive predictive values of the test were calculated.

RESULTS

The total number of neonates estimated with cord bilirubin levels were 656. A total of 89 Neonates who were discharged early from the hospital, the ones who did not turn up for the follow-up for re-estimation of serum bilirubin at 72 hours were excluded from the study. Thus the total no. of neonates included in the study was 567. Cord bilirubin levels coming in different range and number of neonates are shown in table 1.These cord bilirubin values were compared with serum bilirubin values of neonates after 72 hours (table 2).

With Receiver operating characteristic (ROC) analysis, a cutoff value of cord bilirubin level of ≥1.89mg/dL was determined which has the highest sensitivity (96.36%) to predict the newborns who would develop significant hyperbilirubinemia. Of the 201 newborns who had a cord bilirubin level of ≥1.89 mg/dL, 53 (26.4%) developed significant hyperbilirubinemia after 72 hours of life, whereas only 2 of the 366 newborns (0.546%) who had a cord bilirubin level of <1.89mg/dL on the first day developed significant hyperbilirubinemia (table 3) and required phototherapy

The probability that neonates with cord bilirubin higher than 1.89mg/dl would later develop hyperbilirubinemia (Positive Predictive Values) was 26.40% and negative predictive values was 99.45%, Sensitivity was 96.36% and Specificity was 71.09%. These results are shown in table 4. Characteristics of cases who did and who did not develop significant hyperbilirubinemia (≥17mg/dl) after 72hrs with respect to various factors that may be associated with the risk of hyperbilirubinemia, such as gender, gestational age, birth weight, delivery route and haemotocrit level were studied and found as no significant differences between the two groups (table 5). Similarly there were no significant differences between the cases who had cord bilirubin level <1.89mg/dl and >1.89mg/dl with respect to various factors (table 6)

Table 1: Distribution of cord bilirubin levels

Cord Bilirubin Range (mg/dl)	No. of Neonates with Significant Hyperbilirubinemia n(%)
0.4-1	Nil
>1-1.5	Nil
>1.5-2	4(7.27%)
>2	51(92.72%)

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Table 2: Cord biirubin vs No. of neonates with significant hyperbilirubinemia

Cord Bilirubin Range (mg/dl)	No. of Neonates with Significant Hyperbilirubinemia n(%)
0.4-1	Nil
>1-1.5	Nil
>1.5-2	4(7.27%)
>2	51(92.72%)

Table 3: Relationship between cord bilirubin and serum bilirubin after 72hrs

Cord Bilirubin	Neonates with Sr.Bilirubin ≥17mg/dl(n=55)	Neonates with Sr.Bilirubin <17mg/dl(n=512)
>1.89(n=201)	53	148
<1.89(n=366)	2	364

Table 4: Results of analysis

SENSITIVITY	96.36%
SPECFICITY	71.09%
POSITIVE PREDICTIVE VALUE	26.40%
NEGATIVE PREDICTIVE VALUE	99.45%

Table 5: Characteristics of cases who did and who did not develop significant hyperbilirubinemia(≥17mg/dl) after 72hrs

Characteristics	Serum bilirubin (<17mg/dl) after 72hrs	Serum bilirubin (≥17mg/dl) after 72hrs	P value
Males/Females	240/272	27/28	0.754
Gestational Age	38.59±0.818*	38.55±0.715*	0.725
Birth weight	2.838±0.302*	2.859±0.320*	0.635
Mode of delivery			
Normal delivery	243	27	0.708
Caesarean	269	28	0.818
Cord Haematocrit	44.418±5.365*	44.213±5.268*	0.787
Cord Bilirubin	1.625±0.394*	2.390±0.334*	<0.0001

(P value < 0.05 is significant, *= mean ± standard deviation)

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Table 6: Characteristics of cases who had cord bilirubin level of <1.89mg/dl and >1.89mg/dl

Characteristics	Cord bilirubin <1.89mg/dl	Cord bilirubin >1.89mg/dl	P value
Males/Females	171/195	96/105	0.812
Gestational Age	38.60±0.807*	38.54±0.812*	0.386
Birth weight	2.851±0.304*	2.820±0.303*	0.248
Mode of delivery			
Normal delivery	174	96	0.752
Caesarean	192	105	0.960
Cord Haematocrit	44.581±5.675*	44.065±4.702*	0.272

(P value < 0.05 is significant, *= mean ± standard deviation)

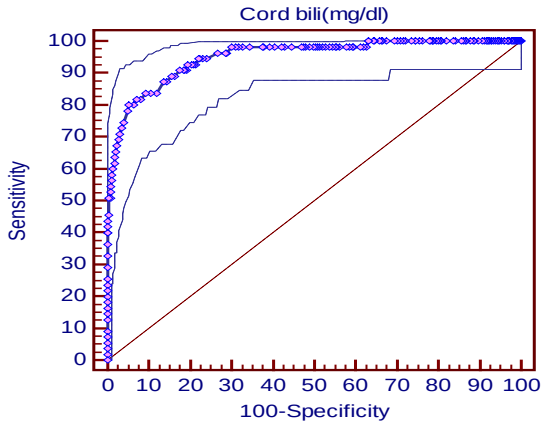

Figure 1: Receiver operating characterstic (ROC) analysis

Table 7: Receiver operating characterstic (ROC) analysis

Area under the ROC curve (AUC)	0.951
Standard Error [a]	0.0148
95% Confidence Interval [b]	0.929 to 0.967
z statistic	30.450
Significance level P (Area=0.5)	<0.0001

DISCUSSION:

Jaundice in newborn is quite common, affecting nearly 60% of term and 80% of preterm neonates during first week of life [6]. Higher cord bilirubin levels among infants who later become jaundiced compared to cord bilirubin levels in non-jaundiced infants indicate that mechanisms of importance for the subsequent jaundice are already active in late fetal life. The maternal and umbilical cord bilirubin concentration at delivery, a yellow skin colour on the first post-natal day, an increase in the yellow skin colour during the first 24 h of postnatal life, and carbon monoxide excretion are all associated with the later development of neonatal jaundice in the healthy, mature newborn infant [7]. The incidence of significant hyperbilirubinemia depends on regional variations, ethnic makeup of the population, laboratory variability in the measurement of bilirubin, and the incidence of breastfeeding.

In our study group, there were no significant differences between the cases who did and the cases who did not develop significant hyper-bilirubinemia with respect to these factors (such a haematocrit level, gender, delivery

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route, birth weight and gestational age) that may be associated with the risk of hyperbilirubinemia Rosenfeld J reported that infants with cord bilirubin levels less than 2.0 mg/dL have only a 4 percent chance of developing hyperbilirubinemia and a 1.4 percent chance of needing phototherapy. However, if serum cord bilirubin levels are more than 2.0 mg/dL, the infant has a 25 percent chance of developing subsequent hyperbili-rubinemia [8].

Rataj J et al reported that if cord bilirubin was under 1 mg%, jaundice occurred in 2.4% newborns, where as 89% of the infants with cord bilirubin above 2.5 mg% became jaundiced [9]. Knudsen A found that if cord bilirubin was below 20 µmol/l(1.17mg/dl), 2.9% became jaundiced as opposed to 85% if cord bilirubin was above 40 µmol/l(2.34mg/dl). Furthermore, 57% of jaundiced infants with cord bilirubin above 40 µmol/l(2.34mg/dl) required phototherapy, but only 9% if cord bilirubin was 40 µmol/l(2.34mg/dl) or lower (p less than 0.003) [10].

Thus it can be seen that different authors have used different cutoff value for predicting significant jaundice. This variability is mainly because of technical error in estimating bilirubin levels. Bilirubin estimation varies from laboratory to laboratory. Hence the cutoff value taken in different studies are different. Therefore it is important that local laboratory should define what is the cutoff value that should be used as a predictor for development of significant jaundice.

In present study, the cord bilirubin level of >1.89 mg/dL had the highest sensitivity (96.36%), and this critical bilirubin level had a very high (99.45%) negative predictive value and fairly low (26.4%) positive predictive value this finding compatible with other studies [11,12]. The cord bilirubin level of <1.89 mg/dL did not completely exclude the development of significant hyperbilirubinemia; only 0.546% of the newborns with cord bilirubin levels of <1.89mg/dL developed jaundice. A 99.45% negative predictive value in the present study suggests that measurement of cord serum bilirubin can help in identify those newborns who are unlikely to require further evaluation and intervention [11,12].

CONCLUSION:

In conclusion estimating cord bilirubin levels is a simple and non invasive screening test to predict those neonates who are at least risk of developing significant hyperbilirubinemia and unlikely to require further evaluation and intervention

Conflict of interest: none

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REFERENCES:

1. Practice Parametre: Management of hyperbilirubinemia in the healthy term newborn. American Academy of Pediatrics. Provisional Committee for Quality Improvement and Subcommittee on Hyperbilirubinemia. Pediatrics. 1994 ;94:558-65.
2. Kiely M, Drum MA, Kessel W. Early discharge. Risks, benefits, and who decides. Clin Perinatol. 1998;25(3):539-53.
3. Maisels MJ, Newman TB Kernicterus in otherwise healthy, breast-fed term newborns. Pediatrics 1995; 96: 730-733.
4. Penn AA,Enzman DR, Han JS, Stevenson DK. Kernicterus in a full term infant. Pediatrics 1994;93: 1003-06.
5. American Academy of Pediatrics. Practice parameter: Management of hyperbilirubinemia in the healthy team newborn. Pediatrics 1994; 94: 558-567.
6. Stoll BJ, Kleigman RM. Jaundice and hyperbilirubinemia in newborn. In: Behrman RE, Kliegman Rm, Jenson HB ed. Nelson Textbook of Pediatrics 16th edn, WB Saunders company, 2000: 513-517
7. Knudsen A. Prediction and noninvasive assessment of neonatal jaundice in the term healthy newborn infant. Acta Paediatr 1996; 85: 393- 397
8. Rosenfeld J. Umbilical cord bilirubin levels as predict-or of subsequent hyperbilirubinemia. J Fam Pract 1986; 23: 556-58
9. Rataj J, Kornacka M, Korman E. Usefulness of meas-uring bilirubin levels in cord blood for predicting hyperbilirubinemia in newborns Ginekol Pol. 1994 Jun; 65:276-280
10. Knudsen A. Prediction of the development of neonatal jaundice by increased umbilical cord blood bilirubin. Acta Paediatr Scand 1989; 78: 217-221
11. Sun G; Wang YL; Liang JF; DU LZ . Predictive value of umbilical cord blood bilirubin level for subsequent neonatal hyperbilirubinemia. Zhonghua Er Ke Za Zhi (Chinese J Ped) 2007; 45 (11): 848-52.
12. Bernalda AJ, Segre C. A Bilirubin dosage in cord blood : Could it predict neonatal hyperbilirubinemia? Sao Paulo Med J 2004; 122 ;99-10317.

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