

Original Research Article

Prediction of neonatal hyperbilirubinemia using umbilical cord blood bilirubin

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Received: 12 February 2019

Accepted: 16 February 2019

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ABSTRACT

Background: Neonatal hyperbilirubinemia is a common problem among newborns. Neonatal hyperbilirubinemia has a potential complication of kernicterus which is still seen in many newborns. In present study authors used umbilical cord blood bilirubin to predict the development of significant hyperbilirubinemia in the early neonatal period. The objective of this study is to evaluate the correlation between concentration of bilirubin in the cord blood and occurrence of hyperbilirubinemia in term newborns.

Methods: In this prospective study authors included 500 term healthy consecutively born babies whose umbilical cord blood was collected and were followed up for first 7 days for the appearance of jaundice. The clinical assessment of jaundice was done by Kramer rule. The data was analyzed by using SPSS 17 statistical software.

Results: Study found that umbilical cord blood bilirubin was 90% sensitive and 87% specific with a PPV of 75% and NPV of 92% in predicting significant neonatal hyperbilirubinemia.

Conclusions: The study conducted clearly points that the use of cord blood bilirubin for identifying newborns at risk of hyperbilirubinemia helps in early detection and treatment of jaundice. There by preventing the potential complication kernicterus. This method is economical and socially acceptable. Hence cord blood bilirubin should be done on all healthy term newborns.

Keywords: Bilirubin, Cord blood, Neonatal jaundice, Phototherapy, Preterm

INTRODUCTION

Jaundice is a clinical condition that is present in pediatric practice and constitutes one of the major issues within the neonatal period. It occurs in both physiological and pathological processes in newborns.¹ Neonatal hyperbilirubinemia is defined as significant when serum bilirubin levels more than or equal to 17mg/dl. Neonatal jaundice may not appear until serum bilirubin exceeds 5-7mg/dl.² Early discharge of newborn after delivery is a common practice because of medico-social reasons and economic constraints. Thus, the recognition,

follow up and treatment of jaundice has become more difficult as a result of early discharge from hospital. An association between decreased length of stay and the risk of re-admission has been shown and the most common cause for re-admission during neonatal period is hyperbilirubinemia.² Concerns regarding early discharge and hyperbilirubinemia in newborn has been subject of many controversies. Early hospital discharge has had the implication of re-examining the approach towards neonatal jaundice, taking into consideration the bilirubin level present in the first 24 hours to 48 hours of life as a means of predicting hyperbilirubinemia.¹

Some degree of jaundice is seen in 60-70% of term and about 80% of preterm newborns. Chemical jaundice (serum bilirubin level 2mg/dl) is universal in newborn. 6.1% of well term newborns have a maximum serum bilirubin over 12.9mg/dl. Serum bilirubin level >15mg/dl is seen in 3% of normal term newborns.³

The American Academy of Pediatrics recommends that newborns discharged within 48 hours should have a follow up visit after 2-3 days for any significant jaundice and other problems. This recommendation is not appropriate for present country due to limited follow up facilities in the community. Therefore, it is difficult to predict which infants are at increased risk for significant and relatively late hyperbilirubinemia.⁴⁻⁶

Treatment of severe neonatal jaundice by exchange transfusion is costly, labor intensive, time consuming and associated with complications. Many a time's appropriate blood is not available. Early treatment of jaundice with phototherapy is effective, simple and cheap. This technology is appropriate in treating neonatal jaundice.

Financial constraints, family and medical consideration shortage of hospital beds and personnel frequently influence the decision about early discharge of the mother and infant after birth. Many newborns who are clinically doing well at the time of discharge, may develop hyperbilirubinemia at a later date. Ignorance on the part of parents may result in late reporting and thereby lead to complications inherent to hyperbilirubinemia.

Hence at the time of discharge, there is a necessity to adopt a method to predict the likely development of hyperbilirubinemia. Early prediction facilitates the use of effective preventive measures and early treatment and thereby reducing mortality and morbidity.

And as such, from the obvious need to design and implement a follow up programme, the present study was conducted to find out the critical value of serum bilirubin in the cord blood in predicting the subsequent development of hyperbilirubinemia in healthy newborn.

METHODS

A hospital based prospective study was conducted on 500 healthy full term newborns born in Vani Vilas Hospital and Bowring and Lady Curzon Hospital attached to Bangalore Medical College and Research Institute during the study period from October 2010 to September 2012.

The cord blood bilirubin estimation will be done at birth and serum bilirubin level will be done after 72 hours of birth. The cord and serum bilirubin estimation will be done using-modified Jendrassik-Grof method, a photometric method for estimation of direct and total bilirubin. All the neonates will be observed for the development of jaundice for at least 5 days.

Inclusion criteria

- Gestational age more than 37 weeks.

Exclusion criteria

- Gestational age less than 37 weeks
- Birth weight less than 2500 grams.
- Newborns with significant illness requiring admission.
- Newborns with major congenital malformations.
- Newborns with blood group incompatibility.

Informed consent was obtained from all the parents of the newborns to be enrolled for the study. In all the newborns, relevant information was collected in a predesigned proforma.

RESULTS

There is concern about increasing incidence of kernicterus in healthy term neonates and hyperbilirubinemia is one of the most common cause of hospital re admission of the term newborn. Early detection of hyperbilirubinemia in the early discharged newborn from the hospital is therefore important. Knowledge of the infant at risk of developing hyperbilirubinemia allows simple bilirubin reducing methods to be implemented before critical levels are reached.

Table 1: Social profile of study participants.

		Number of newborns	Percentage
Birth weight (kg)	2.5-3.5	475	95.0
	>3.5	25	5.0
Gender	Male	266	53.2
	Female	234	46.8
Gestational hypertension	Present	168	33.6
	Absent	331	66.2
Mode of delivery	Vaginal	197	39.4
	Caesarian section	303	60.6
Blood Group	A	151	30.2
	B	238	47.6
	AB	55	11
	O	56	11.2
Parity	Primi	323	64.6
	Multi	177	35.4

The male: female ratio in the present study was found to be 1.13:1, with 53.2% male and 46.8 % female were included in the study. In the present study 33.8% of the mother had gestational hypertension. In the present study babies born by vaginal delivery and caesarian section were 39.4% and 60.6% respectively. In the present study blood group B was more among the neonates followed by A, O and AB. In the present study 64.6% of mothers were

prim gravida (Table 1). The bilirubin level on day 3 was found to be statistically not significant with the variables

like parity, mode of delivery, gestational hypertension, blood group, birth weight and gender (Table 2).

Table 2: Distribution of study participants based on D 3 bilirubin values.

		D3 bilirubin mg/dl				P value
		<17mg/dl		>17mg/dl		
		N	Percentage	N	Percentage	
Gender	Male	195	51.4	71	58.6	0.175
	Female	184	48.5	50	41.3	
Gestation HTN	Without hypertension	248	65.4	83	68.5	0.582
	With hypertension	130	34.3	38	31.4	
Mode of Delivery	Vaginal delivery	148	39	49	40.4	0.831
	Caesarian section	231	60.9	72	59.5	
Birth weight (kg)	2.5-3.5	358	94.5	117	96.7	0.32
	>3.5	21	5.5	4	3.3	
Blood group	A	114	30.0	37	30.5	0.187
	B	43	11.3	12	9.9	
	AB	187	49.3	51	42.1	
	O	35	9.2	21	17.3	
Parity	Primi	245	64.6	78	64.4	0.971
	Multi	134	35.3	43	35.5	

The cord bilirubin level of more than 1.78mg/dl was seen in 67.6% of the study participants and bilirubin level of more than 17mg/dl was seen in 75.8% of the newborns. In present study nearly 90.9% of the study subjects had cord bilirubin level more than 1.78mg/dl and Bilirubin level of more than 13mg/dl. In the present study there was statistically significant association between cord bilirubin level of ≥ 1.78 mg/dl and development of neonatal hyperbilirubinemia ($p < 0.001$) * (Table 3).

Table 3: Distribution of cord bilirubin among newborns with D3 bilirubin level ≥ 17 mg/dl.

Cord bilirubin (mg/dl)	D3 bilirubin mg/dl ≥ 17 mg/dl	
	N	Percentage
<1.78	11	9.1
≥ 1.78	110	90.9
Total	121	100.0

Table 4: Cord blood bilirubin level (mg/dl) as diagnostic marker for predicting the development of neonatal hyperbilirubinemia.

Parameter	Number of newborns (n=500)	Percentage
Number of newborns with D3 bilirubin level of ≥ 17 mg/dl	121	24.2
Number of newborns with cord blood bilirubin ≥ 1.78 mg/dl	162	32.4
Number of newborns with Cord blood ≥ 1.78 mg/dl and D3 bilirubin level of ≥ 17 mg/dl	110	22.0
Sensitivity %	90.91	
Specificity %	86.28	
PPV %	85.79	
NPV %	96.75	
Accuracy %	87.14	
AUC	0.948*	

In the present study cord serum bilirubin of ≥ 1.78 mg/dl was having the sensitivity of 90.91%, specificity of 86.28%, positive predictive value of 85.79%, and negative predictive value of 96.75% in the prediction of

neonatal hyperbilirubinemia. ($p < 0.001$). The area under the curve was found to be 0.948 in ROC with p value showing statistically significant (Table 4 and Figure 1).

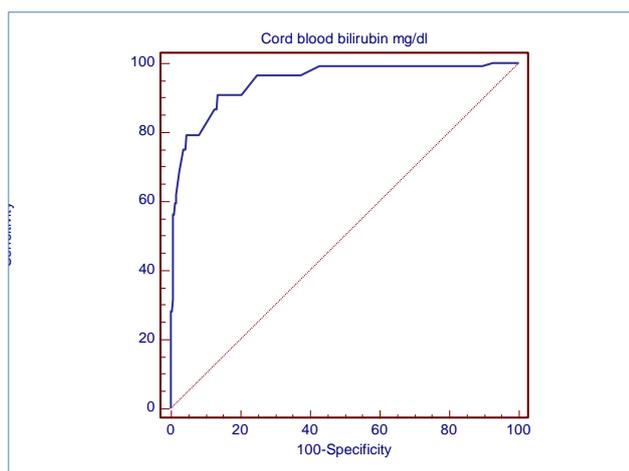


Figure 1: Graph showing receiver operating characteristics (ROC) curve.

DISCUSSION

Jaundice is a clinical condition that is present in pediatric practice and constitutes one of the major issues within the neonatal period. It occurs in both physiological and pathological processes in newborns.¹ Early discharge of newborn after delivery is a common practice because of medico-social reasons and economic constraints. An association between decreased length of stay and the risk of re-admission has been shown and the most common cause for re-admission during neonatal period is hyperbilirubinemia.² The potential risk of developing bilirubin encephalopathy or even kernicterus is high in babies with elevated serum bilirubin level. The sequel could be serious as patients may develop cerebral palsy, sensorineural deafness and mental retardation. Hence, there is a necessity to adopt a method to predict the likely development of hyperbilirubinemia. Early prediction facilitates the use of effective preventive measures and early treatment and thereby reducing mortality and morbidity. A prospective, correlation study with 500 newborns is undertaken to study the predictive potential of cord blood bilirubin as marker to predict the hyperbilirubinemia.

the present study infers that the neonatal hyperbilirubinemia is independent of the sex of the newborn. In a similar study conducted by Taksande A et al in 2005 on 200 neonates comprising of 82 males and 118 females ($p=0.323$) it was observed that no significant correlation existed between the sex of the newborn and the neonatal hyperbilirubinemia ($\geq 17\text{mg/dl}$).² In 2005 Rostami et al in a study conducted on 643 healthy term newborns in Iran concluded that there is no correlation between the neonatal hyperbilirubinemia and sex of the newborn.⁷ Satrya R et al in 2009, in their study showed significant correlation between the sex of the newborn and neonatal hyperbilirubinemia with $p < 0.05$.⁸

There is no statistically significant association between the neonatal hyperbilirubinemia ($\geq 17\text{mg/dl}$) and the mode

of the delivery ($p=0.821$) which was similar to findings of Knudsen et al and Taksand A et al and Awasthi et al.^{2,9,10}

In the present study there was no significant association between the neonatal hyperbilirubinemia and gestational hypertension which is similar to the studies conducted by Awasthi et al and Taksande A et al with p value of 0.5 and 0.06 respectively.^{2,10}

In the present study there was no significant association between the birth weight and development of neonatal hyperbilirubinemia. Taksande A et al, in their study on 200 healthy term neonates did not observe significant association between birth weight and development of neonatal hyperbilirubinemia.² Similarly, Satrya R et al 2009, in their study on 88 healthy term newborns found no association between the birth weight and development of neonatal hyperbilirubinemia.⁸

In the present study there was no correlation between the blood group of neonates and development of neonatal hyperbilirubinemia. Satrya R et al, in their study conducted on 88 healthy term newborns found no association between blood group and neonatal hyperbilirubinemia which is similar to the present study.⁸

In the present study there was no significant association between the parity and development of neonatal hyperbilirubinemia which is similar to the findings of study conducted by Satrya R et al.⁸

In the present study, critical cord bilirubin level ($\geq 1.78\text{mg/dl}$) with high sensitivity and specificity was selected based on ROC curve analysis. The probability that a newborn with cord blood bilirubin $\geq 1.78\text{mg/dl}$ would later develop hyperbilirubinemia was 85.28% (positive predictive value). The negative predictive value, the probability of not developing hyperbilirubinemia when cord bilirubin level is $< 1.78\text{mg/dl}$ was 96.75%. If a child develops hyperbilirubinemia, the probability that the cord bilirubin level was $\geq 1.78\text{mg/dl}$ was 90.91% (sensitivity). When a newborn did not develop hyperbilirubinemia then the probability that the cord bilirubin level $< 1.78\text{mg/dl}$ was 86.28% (specificity). Several studies are published on the usefulness of the cord bilirubin concentration in prediction of hyperbilirubinemia. Knudsen et al, observed that if the cord bilirubin level was below $< 20\mu\text{mol/l}$ (1.17mg/dl), 2.9% newborns developed hyperbilirubinemia as opposed to 85% if the cord bilirubin was above $40\mu\text{mol/l}$ (2.35mg/dl) and 57% of them with cord bilirubin above $40\mu\text{mol/l}$ (2.35mg/dl) required phototherapy. Taksande A et al, showed that the cord bilirubin level $> 2\text{mg/dl}$ has a sensitivity of 89.5%, specificity of 85% and negative predictive value of 98.7% which is in correlation with present study except the positive predictive value of (38.8%).² Nahar Z et al showed that the cord bilirubin level of $> 2.5\text{mg/dl}$ has a sensitivity of 77%, specificity of 98.6% and negative predictive value of 96% which is in accordance with the present study.⁴ The observations of

the studies of Sun G et al and Satrya R et al are also in accordance with present study.^{8,11}

Rostami et al in their study to identify healthy newborn at risk for developing significant hyperbilirubinemia (>14mg/dl) by measuring cord bilirubin level in 643 term babies, concluded that cord serum bilirubin cannot identify newborn with subsequent significant hyperbilirubinemia.⁷ The variations in the value of cord bilirubin that predicts significant hyperbilirubinemia can be explained by the differences in the sample size, method of estimation of bilirubin and duration between the collection and estimation of bilirubin and by their chosen cut off values for significant neonatal hyperbilirubinemia.

CONCLUSION

Estimation of cord blood bilirubin is simple, inexpensive and effective tool in screening babies for the development of neonatal hyperbilirubinemia, especially in a large hospital setting with large number of deliveries, where pressure for discharging the mother and the baby early is high.

Universal screening of cord blood bilirubin should be done in all term babies to predict the development of significant neonatal hyperbilirubinemia.

This in turn will aid in early intervention and prevent the dangerous consequence of neonatal hyperbilirubinemia that is kernicterus.

Thus, the morbidity and mortality due to neonatal hyperbilirubinemia can be minimized.

Estimation of cord blood bilirubin level not only will enable the treating pediatrician in decision making regarding the discharge and need for follow up on day 3 for the development of significant hyperbilirubinemia in the event of early discharge from the hospital but also will help in counselling of the parents.

Limitation of the study: preterm infants were not included in the study, hence needs a separate study to know the cord blood bilirubin value to predict the neonatal hyperbilirubinemia in preterm babies.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Haridas K, Shinde R, Belavadi G. Prediction of neonatal hyperbilirubinemia using umbilical cord blood bilirubin. Int J Contemp Pediatr 2019;6:248-52.