



## PREDICTIVE VALUE OF UMBILICAL CORD BILIRUBIN IN OCCURRENCE OF HYPERBILIRUBINEMIA IN NEONATES

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### ABSTRACT

**Objectives:** Neonatal hyperbilirubinemia (NH) is a universal problem affecting nearly 60% of term and 80% of preterm neonates during first week of life. Early discharge of healthy term newborns is a common practice because of medical, social and economic constraints. In significant number (6.5%) of babies, NH is a cause for readmission. The present study was conducted to correlate the Cord Blood Bilirubin (CBB) level with subsequent NH.

**Methods:** Study was performed at the Department of Pediatrics in a Rajah Muthiah Medical College Hospital. 150 full-term newborns during 1-year period, were prospectively enrolled. CBB was estimated. Serum Bilirubin estimation was done at 72 hours of age and later if required.

**Results:** Significant NH in our study is 1.3 %. Mean total bilirubin on third post natal day was 10.06 mg/dl. Using CBB level of 3 mg/dl as a cut-off, NH can be predicted with sensitivity of 100%, specificity of 99 %, positive predictive value of 66 % and negative predictive value of 100%.

**Interpretation & Conclusion:** A 100% Negative Predictive Value in the present study suggests that in Healthy Term babies (without RH and ABO incompatibility with Cord Blood Bilirubin 3 mg/dl ) cord serum bilirubin can help to identify those newborns who are unlikely to require further evaluation and intervention. These newborns can be discharged with assurance to Parents. Babies with CBB level 3 mg/dl should be followed more frequently.

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## INTRODUCTION

Jaundice in newborn is a universal problem about which we have been talking and worrying for more than a century. Neonatal hyperbilirubinemia remains a public health concern as documented by recent reports of kernicterus in otherwise healthy term and near-term newborns. Kernicterus in such New-borns is preventable, provided excessive hyperbilirubinemia for age is promptly identified and appropriately treated.<sup>1,2</sup> With the intent to facilitate such identification and treatment, universal screening for severity of bilirubinemia before hospital discharge may predict that extraordinary segment of the neonatal population which is at risk for excessive hyperbilirubinemia during the first week after birth.<sup>3</sup> It affects nearly 60% of term and 80% of preterm neonates during first week of life.<sup>4</sup> Neonatal hyperbilirubinemia (NH) is a cause of concern for the parents as well as for the pediatricians.<sup>5</sup>

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 minimize the risk of bilirubin dependent brain damage. The present study was conducted to evaluate the predictive value of cord bilirubin level for identifying term infants for subsequent hyperbilirubinemia

## MATERIALS

This study was performed at the Department of Pediatrics of Rajah Muthiah Medical College & Hospital. Full-term newborns 150 in numbers born at this hospital during 1-year period was prospectively enrolled in the study. The study was approved by the Research Ethics Committee of Rajah Muthiah Medical College & Hospital. **INCLUSION CRITERIA :** Gestation >37weeks. **EXCLUSION CRITERIA**

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:Significant illness requiring NICU admission, Major congenital malformations.

**Method Of Collection Of Data**

The demographic profile and relevant information of individual patient was collected by using structured Proforma by interviewing the mother. Gestational age was assessed by New Ballard score. CBB was estimated. Serum Bilirubin estimation was done at 72 hours of age. All babies were followed up daily for the first five postnatal days.

**Laboratory Investigation**

- Two (2) ml each of plain and EDTA cord blood sample was collected from placental side after its Separation and subjected to following investigation.

**Blood group**

Total and direct serum bilirubin.

- Two (2) ml each of plain and EDTA venous blood samples were collected from the baby on 72 hours of life. These samples were subjected to following investigation.

Total and direct serum bilirubin.

Blood collected was transported to laboratory within two hours of collection.

Serum bilirubin estimation was done by Diazo method. This method for bilirubin estimation is based on principle that Bilirubin reacts with diazotised sulphanilic acid in acidic medium to form pink coloured azobilirubin with absorbance directly proportional to bilirubin concentration. Direct Bilirubin, being water soluble directly reacts in acidic medium. However indirect or unconjugated Bilirubin is solubilised using a surfactant and then it reacts similar to direct Bilirubin.

**RESULTS**

A Prospective study consisted of 150 term newborns delivered in Rmmch

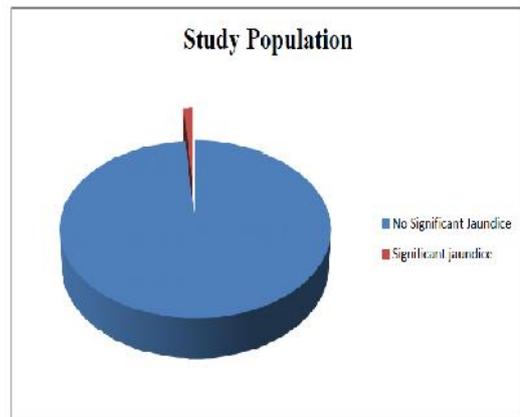
**Table 1 Study Population And Significant Jaundice**

Total	Significant Jaundice	
	Number	Percentage
150	2	1.3 %

The incidence of significant hyperbilirubinemia in our study population is 1.3 %. Significant jaundice is defined as TSB 15 mg/ dl at 72 hours of life.

The baseline maternal data of 150 neonates is shown in the above table. According to the age of the mother the study population was divided into three groups. First group constitutes in the age group of 18 – 20 (34.7%), Second group constitutes in the age group of 21 – 30 (64

%) and the last group is 31 – 40 (1.3%). The primi and multi were equally distributed in our study population. We have included O type babies born to O+ mothers in our study. The predominant blood group among the mothers was the B type, found in 62 cases (41.3%), followed by the A type in 40 cases (26.7%), O type in 37 cases (24.7%) and AB type in 11 cases (7.3%).



Graph 1 Study Population and Significant Jaundice

**Table 2 Maternal Details (N = 150)**

Mother details	Number of mothers	Total %	Significant Jaundice %
Mother age in years			
• 18-20	52	34.7	1.9
• 21-30	96	64.0	1.0
• 31-40	2	1.3	Nil
Parity			
• Primi	75	50.0	2.6
• Multi	75	50.0	Nil
Blood group			
• A+	40	26.7	2.5
• B+	62	41.3	1.6
• O+	37	24.7	Nil
• AB+	11	7.3	Nil
Total	150	100.0	

**Table 3 Details of Neonates Studied**

Mother details	Number of mothers	Total %	Significant Jaundice %
Gender			
• Male	75	50.0	1.3
• Female	75	50.0	1.3
Weeks of Gestation			
• 37-38	133	88.6	1.5
• 39-40	17	11.4	Nil
Birth weight (kg)			
• 2.50-3.00	109	72.6	1.8
• 3.01-3.50	39	26.0	Nil
• 3.51-4.00	2	1.4	Nil
Bloodgroup			
• A+	33	22.0	Nil
• B+	60	40.0	1.6
• O+	47	31.3	2.1
• AB+	10	6.7	Nil
Total	150	100.0	

In this study, the numbers of male and female babies were equally distributed. This implies uniform sex distribution in the study group. Majority of the babies that is 76% of the study population were of 37 – 38 weeks of gestation. Similarly majority of the babies that is 62.3% of the babies birth weight were between 2.5 – 3 kg. We have included O type babies born to O+

mothers in our study. The predominant blood group among the newborns was also the B type, found in 60 babies (40%), followed by the O type in 47 cases (31.3%), A type in 33 cases (22%) and AB type in 10 cases (6.7%).

**Table 4** Comparative Evaluations of Cord and Day 3 Total Bilirubin

	Cord	Day 3
Total Bilirubin	2.01±0.45	10.06±2.16

Mean cord bilirubin level was 2.01 mg/dl. There was an increase in serum bilirubin level on each day and the mean total bilirubin on third post natal day was mg/dl.

**Table 5** Diagnostic Predictability of Cord Blood Total Bilirubin of >3 Mg/Dl For Hyperbilirubinemia at 72 Hours

Diagnostic statistics	
True Positive	2
False Positive	1
False negative	0
True negative	147
Sensitivity (%)	100
Specificity (%)	99
PPV (%)	66
NPV (%)	100
Accuracy (%)	99.3

In this study probability that a neonate with cord bilirubin higher than 3 mg/dl would later develop hyperbilirubinemia (Positive Predictive Values) was 66 %. The negative predictive value of the cord bilirubin lower or equal to 3 mg/dl was 100%. If a neonate becomes hyperbilirubinemic, the probability that the cord bilirubin was higher than 3 mg/dl was 100% (Sensitivity). The probability that the cord bilirubin was lower or equal to 3 mg/dl was 99 % (Specificity) in a Non hyperbilirubinemic neonate.

## DISCUSSION

Serum bilirubin levels are usually 1-3 mg/ dl at birth and rise at the rate of less than 5 mg/ dl per day, peaking at 2-3 days in term neonates. Our study hypothesis was that a high serum bilirubin level at birth would also predict a high peak later in life. Our aim was to quantify the relationship between Cord blood bilirubin with peak serum bilirubin levels of the first five days. We chose cord blood estimation for initial serum bilirubin estimation because it is a non invasive way and the results are available within few hours after birth

The growing practice of early discharge of newborns resulted in a re- emergence of bilirubin related neurological sequelae. Therefore, it is important to establish safe markers to detect babies at risk for significant hyperbilirubinemia. Development of safe marker will help in preventing fatal outcome due to jaundice.

To address this issue AAP recommends that follow up should be provided to all neonates discharged less than 48 hours after birth by a health care professional in an office, clinic, or at home within 2 to 3 days of discharge.

Compliance with this advice may not be easy however, particularly in rural or lower socioeconomic areas, and given the rarity of kernicterus, it will be very difficult, if not possible to document the benefits of this policy.

Experience suggests that asking mothers to observe infants for the development of jaundice is not satisfactory. Despite such instructions, it is difficult for many parents to recognize significant jaundice. Unfortunately, the presence of excessive jaundice for age is often missed clinically, which means that the trigger for measuring the first serum bilirubin level and electing subsequent recommendation is not set. This is a potentially a serious problem. Variability in the time of appearance of jaundice from newborn to newborn and in the ability of the professionals to see jaundice and estimate its severity, coupled with the considerable range of TSB values associated with its cephalo-caudal progression, have been the subject of articles spanning nearly 60 years. Even in the landmark Bhutani et al study, with health care providers sensitized to the significance of clinical jaundice, there were several instances when its early appearance was missed (often attributable to confounding skin colour). Additionally in most of the recently reported healthy term newborns who developed kernicterus, significant jaundice was almost certainly present before the first hospital discharge, judging from the height of TSB for age in hours at readmission. Either the early icterus had not been noted or its pathologic intensity for postnatal age was not appreciated.

Currently we do not have a reliable method of anticipating such levels of hyperbilirubinemia. It is possible that closer, and more frequent, follow up after birth and discharge from the hospital might prevent some of these unfortunate outcomes, but rare, sporadic cases of kernicterus may not be preventable unless we adopt an approach to surveillance of the newborn that is substantially more rigorous than has been practiced. The feasibility, costs, risks and benefits of such an approach need to be determined. Umbilical cord blood collection is not associated with any pain. Furthermore, most important is that the data are available immediately after birth. 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. The use of Cord blood bilirubin values may help to predict infants with low risk for hyperbilirubinemia and minimise an unnecessary prolongation of hospitalization.

Keeping these factors in consideration our study was conducted on term neonates with non-haemolytic jaundice. The outcome was hyperbilirubinemia. We have considered peak serum bilirubin level >15 mg/dl at 72 hours of age as significant hyperbilirubinemia since specific treatment is considered at or above this level

## CONCLUSION

Neonatal hyperbilirubinemia occurs in 5-10% of healthy term infants. Up to 4% of term newborns who

are readmitted to the hospital during their first week of life, approximately 85% are readmitted for jaundice. Early identification of newborn at risk for significant hyperbilirubinemia by using simple predictors can help to prevent possible bilirubin induced neurological dysfunction. A 100% Negative Predictive Value in the present study suggests that in Healthy Term babies (without RH and ABO incompatibility with Cord Blood Bilirubin  $< 3$  mg/dl ) cord serum bilirubin can help to identify those newborns who are unlikely to require further evaluation and intervention. Babies with Cord Blood Bilirubin level  $> 3$  mg/dl should be followed more frequently to reduce mortality and morbidity due to Neonatal hyperbilirubinemia. Thus prediction of neonatal hyperbilirubinemia will have widespread implication especially in our setup where there are limited resources. Healthy newborns at low risk for hyperbilirubinemia can be discharged early from the hospital

#### SUMMARY

The study group consisted of 150 neonates delivered in RMMCH. Cord blood bilirubin and Total Serum Bilirubin at 72 hours was estimated for all neonates. For the first five postnatal days, all these babies in the study group, were followed up daily for clinical assessment of icterus. Incidence of significant hyperbilirubinemia ( TSB  $> 15$  mg/ dl at 72 hours of age ) in our study population is 1.3 %. There was uniform sex distribution in the study group. There were no significant differences between the cases who had cord bilirubin level  $< 3$  mg/dl and  $> 3$  mg/dl with respect to various factors that may be associated with the risk of hyperbilirubinemia, such as gender, gestational age, birth weight, maternal risk. Mean cord bilirubin level was 2.01 mg/dl. Mean total bilirubin on third post natal day was 10.06 mg/dl. There was a

positive correlation between cord bilirubin and third postnatal day serum bilirubin.

Using cord bilirubin level of  $< 3$  mg/dl, Hyperbilirubinemia can be predicted with sensitivity of 100%, specificity of 99 %, positive predictive value of 66 % and negative predictive value of 100%. Healthy term babies without RH and ABO incompatibility with Cord Blood Bilirubin  $< 3$  mg/dl are unlikely to require further evaluation and intervention hence these newborns can be discharged with assurance to Parents. Babies with Cord Blood Bilirubin level  $> 3$  mg/dl should be followed more frequently

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