Incidence of significant jaundice in healthy term newborns and the ability of first two hour bilirubin levels to predict the incidence of significant jaundice.

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Abstract: *Neonatal hyperbilirubinemia is a major problem among newborns occurring in 5-10% of healthy term infants. It is the most common cause of re-admission during early neonatal period in significant number of babies. Severe jaundice can lead to kernicterus causing permanent brain damage. Hence there is an obvious need to predict which infants are at risk of developing significant hyperbilirubinemia. We have conducted a cross-sectional study among 200 healthy term neonates born in Aarupadai veedu medical college and hospital and serum bilirubin levels in the first two hours of life and on fifth postnatal day were estimated. The incidence of significant hyperbilirubinemia in our study is found to be 11%. Neonates were classified into four groups based on serum bilirubin levels at first two hours of life and statistically significant association was found between first two hour of serum bilirubin and incidence of significant jaundice [p <0.0001]. Using first two hour serum bilirubin levels [>2mg/dl], significant hyperbilirubinemia could be predicted with sensitivity of 90.9%, specificity of 84.8%, positive predictive value of 42.5% and negative predictive value of 98.69%.*
Keywords: *hyperbilirubinemia, kernicterus, serum bilirubin, sensitivity, specificity.*

I. Introduction

Neonatal hyperbilirubinemia is a cause of concern for the parents as well as for the pediatricians. It occurs in 5-10% healthy term infants.[1,2] It is most common reason for re-admission after early hospital discharge.[3] Concerns regarding jaundice have increased after reports of bilirubin encephalopathy occurring in healthy term infants without hemolysis who were discharged early.[4] Kernicterus occurs in 9.8% of healthy term infants with total serum bilirubin value of 20 to 25 mg/dl.[4,5]

It is difficult to predict which infants are at increased risk for developing significant hyperbilirubinemia (Total bilirubin > 17 mg/dL). Total serum bilirubin (TSB) in infants discharged within 48 hours of age, generally shows an increasing trend and some of these infants later develop significant hyperbilirubinemia requiring treatment. 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.

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 [7-10]. Out of the first five postnatal days, first day serum bilirubin values have best predictive potential.[8] Serum bilirubin levels in the first two hours of life is safe, simple because sample can be collected from the umbilical cord and it will help in identifying the problem early.

II. Aims and objectives

To calculate the incidence of significant jaundice among the study population and to evaluate whether bilirubin levels in first two hours of life can predict development of significant hyperbilirubinemia (Total serum bilirubin ≥ 17 mg/dL) that would require treatment in full term newborn in the first five days after birth.

III. Material and Methods

This was a cross-sectional study carried out in Aarupadai veedu medical college, Puducherry among 200 healthy term neonates born during the period of July 2012 to July 2014 . Sample size has been calculated based on 80% of average of past three years. Neonates with congenital malformations, fetal hemolytic disease, hydrops fetalis, known viral infection, those with history of maternal syphilis , maternal diabetes, Pre-eclampsia / HELLP syndrome , maternal hepatitis or born to mothers who are oxytocin induced during the delivery were excluded from the study group. The demographic profile and relevant information of individual patient was

collected by using structured proforma by interviewing the mother and an informed consent was obtained. Gestational age was assessed by New Ballard score.

A cord blood sample [2ml] was collected from placental side after its separation. Sample was also collected by venipuncture if cord blood could not be collected and estimated for total and direct serum bilirubin. Two (2) ml each of plain and EDTA venous blood samples were collected from the baby on fifth day or early if brought by parents, depending on clinical situation and transported to laboratory within two hours of collection for evaluation of blood group, total and direct serum bilirubin. Serum bilirubin estimation was done by Malloy and Evelyn method using Technicon-RA50 semi-autoanalyzer based on Vanderberg reaction. Babies were classified into four groups depending on the serum bilirubin levels in the first two hours of life i.e. < 0.9 mg% (group-I), 1.01.9 mg% (group-II), 2.0-2.9 mg% (group-III), > 3 mg% (group-IV). The results were analyzed using sensitivity, specificity, positive predictive value, negative predictive value. The study attained clearance from the institutional ethical committee.

IV.   Results

The incidence of significant hyperbilirubinemia [17mg/dl] in our study population is 11% [table no.I.].

Table No.I: Incidence of significant hyperbilirubinemia

Study population	Significant jaundice[17mg/dl]	
	Number	Percentage
200	22	11%

The study population was grouped into four based on the levels of serum bilirubin levels in the first two hours of life and their relation with incidence of significant hyperbilirubinemia is tabulated as in table .no .II.

Table. No.II. Relation of serum bilirubin levels in the first two hours of life and incidence of significant jaundice.

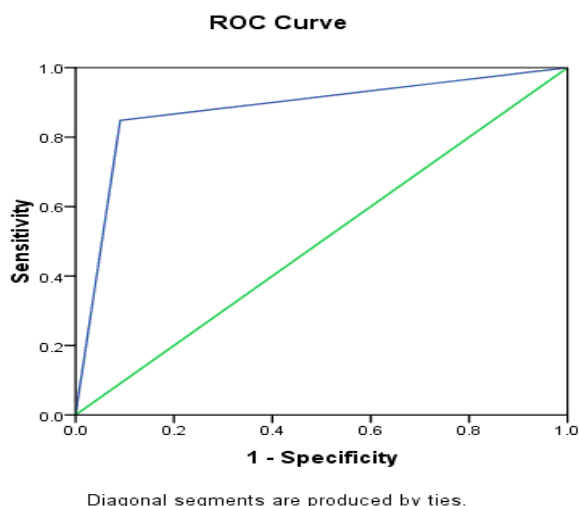| Group	Sr. Bilirubin levels in the First two hrs of life (mg%)	No. of cases of Significant Jaundice	Total No. of cases	Percentage
Group 1	0.0 — 0.9	0	01	0.00
Group II	1.0 —1.9	02	152	1.32
Group III	2.0 — 2.9	12	38	31.58
Group IV	≥3	8	09	88.89
Total		22	200	100

p < 0.0001

The incidence of significant jaundice in group III and IV were 33.58% and 88.89% respectively. There is a statistically significant association between increasing levels of serum bilirubin in the first two hours of life and significant jaundice developing in the first five days (p<0.0001).

Table No.III. Comparision of Incidence of significant jaundice among neonates with varying serum bilirubin levels in first two hours of life.

Serum bilirubin level in the first two hrs of life	No. of cases developed Significant jaundice [17mg/dl]	Total no. of cases
≥2.0 mg/dL	20[42.55%]	47
<2.0 mg/dL	2[1.03%]	153
Total	22[11%]	200

Table. No. IV. Ability of increased serum bilirubin levels in the first two hours of life to predict the incidence of significant jaundice.

Diagnostic test	Value
Sensitivity	90.90
Specificity	84.83
Positive Predictive	42.55
Negative Predictive	98.69

ROC Curve

Diagonal segments are produced by ties.

Area Under the Curve is 0.879
Test Result Variable(s): direct serum bilirubin < 2 hrs of life

In the present study using serum bilirubin levels >2mg/dL in the first two hours of life, hyperbilirubinemia could be predicted with sensitivity of 90.90 %, specificity of 84.83 %, positive predictive value of 42.55 % and negative predictive value of 98.69 %.

V. Discussion

The growing practice of early discharge of newborns resulted in a reemergence of bilirubin related neurological sequelae. Therefore, it is important to establish safe markers to detect babies at risk for significant hyperbilirubinemia inorder to prevent its complications.

Various methods like visual assessment[9] of the newborns during the followup visit after 2 to 3 days of early discharge, first day serum bilirubin estimation,[6,10] predischarge hour specific bilirubin estimation,[7] transcutaneous bilirubin measurement,[11,12] ETCOc measurement[13] and cord blood bilirubin estimation[13,14,15] are used to predict development of significant hyperbilirubinemia. Serum bilirubin estimation in the first two hours of life is safe, simple and it will help in identifying the problem early. The babies at risk for developing significant hyperbilirubinemia can be detected even if parents would like to leave the hospital within the first few postnatal hours.

In the present study , the incidence of significant hyperbilirubinemia is 11%, which is lower comparable to reports by Aplay et al[5] (12.05%) in the year 2000 among 498 study population and Awasthi et al[17] (12.80%) in the year 1998 among 274 study population and higher comparable to reports by Knuffer et al [16] [10.60%] in the year 2005 among 1100 study population.

Present study shows that number of babies developing significant jaundice in the first five days of life increased as the serum bilirubin levels in the first two hours of life increased from group I to group IV as tabulated in table.no.II. There is a statistically significant (p= <0.0001) association between increasing levels of first two hours serum bilirubin levels and incidence of significant jaundice developing in the five postnatal days.Knudsen et al[19] , Bernaldo et al[18] and Knuffer et al[16] in their studies also reported significant relation between increased levels of first two hours serum bilirubin and increased incidence of significant hyperbilirubinemia in the immediate postnatal period.

In the present study using serum bilirubin levels > 2 mg/dL in the first two hours of life, hyperbilirubinemia could be predicted with sensitivity of 90.90%, specificity of 84.83 %, positive predictive value of 42.55 % and Negative Predictive value of 98.69 %. The correlation between first hours bilirubin and development of significant jaundice in the first five days is statistically significant (p<0.0001) . The results in various studies are listed in table .no.V.

Table No. V: Comparison of predictive ability of serum bilirubin level in the first two hours of life

Study	Present Study (%)	Knuffer et al[16] (%)	Knudsen et al[8] (%)
Serum bilirubin level in the first two hours of life	>2.0	≥1.74	≥2.33
Sensitivity	90.90	97.0	13.0
Specificity	84.83	41.40	99.0
PPV	42.55	4.80	85.0
NPV	98.69	99.80	72.00

We couldn't compare predictive ability of first two hours serum bilirubin level (>2 mgdL) of our study with others because the cut –off values each study are different.

VI.   Limitations of the present study
• Since it is hospital based study, it is not feasible to extrapolate the results to community as many factors may influence development of significant jaundice.
• Study involved only term healthy newborns therefore it cannot be generalized to whole neonatal population.
• Two hours bilirubin sample in this study is heterogeneous (Cord blood and venipuncture). We don't know the influence of this on the outcome of the study.

VII.   Summary
• The study group consisted of 200 full-term healthy neonates delivered at AVMC Hospital, Puducherry.
• All babies were followed up for the first five postnatal days.
• Incidence of significant hyperbilirubinemia in our study population is 11%
• Mean serum bilirubin levels in the first two hours of life was 2.23+1.12 mg/dL.
• There is statistically significant association between significant jaundice and increasing serum bilirubin levels in the first two hours of life (p <0.0001).
• Using cut-off serum bilirubin levels of > 2 mg/dL in the first two hours of life, hyperbilirubinemia could be predicted with sensitivity of 90.90%, specificity of 84.83 %, positive predictive value of 42.85%, negative predictive value of 98.69 % and p<0.0001 (Statistically significant).

VIII.   Conclusion
Neonatal hyperbilirubinemia occurs in 5 – 10% of healthy term infants and is the most common reason for readmission after early hospital discharge. Ignorance on the part of parents may result in late reporting to the hospital there by leading to complications inherent with hyperbilirubinemia.

Early identification of newborn at risk for significant hyperbilirubinemia by using simple predictors can help to prevent bilirubin induced neurological dysfunction. Our data suggest that the measurement of serum bilirubin levels in the first two hours of life is a useful tool for early prediction of the subsequent course of jaundice in healthy term newborns. It may help to improve the management of jaundice and thereby prevent its complications.

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