Prediction of Hyperbilirubinemia in Preterm Newborns Admitted in a Tertiary Care Teaching Hospital

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Abstract

Introduction: *Neonatal hyperbilirubinemia is a cause of major concern for the parents as well as the pediatricians due to chance of neurotoxicity. Early prediction of development of significant hyperbilirubinemia can reduce anxiety and duration of hospital stay.*

Objective: *To find out the risk of development of significant hyperbilirubinemia among preterm newborn within first seven days of life.*

Methodology: *This prospective study was carried out in Dhaka Shishu Hospital during the period of January to June, 2007. One hundred & eleven preterm newborns of 30-37 weeks gestational age were enrolled in first day of their life and their serum total and indirect bilirubin were estimated on the 1st, 2nd, 5th & 7th day. Neonates with evidence of hemolysis, direct hyperbilirubinemia, sepsis & major congenital malformation were excluded. Their 1st and 2nd day serum total bilirubin values were analyzed statistically at different cut off points from which significant hyperbilirubinemia can develop on 5th & 7th day of life.*

Results: *The study included 111 premature neonates of 30-37 weeks gestation who were enrolled on first day of their life. Their mean gestational age was 33.7(±2) weeks and mean birth weight was 1754(±341) gm. Of them, 38 (34%) neonates developed significant hyperbilirubinemia within first seven days of life. Among the study population, 40 (36%) neonates had serum total bilirubin value of <2 mg/dL on first day of life. None of them developed significant hyperbilirubinemia (100% negative predictive value). Again 65 (58.5%) neonates had serum total bilirubin value of <5 mg/dL on second day of life. Among them only 7.6% developed significant hyperbilirubinemia (92.3% negative predictive value).*

Conclusion: *The first and second day serum total bilirubin values can predict subsequent hyperbilirubinemia within seven days of life. First day serum total bilirubin value of 2 mg/dL can be taken as a safe limit from which chance of significant hyperbilirubinemia is less.*

Key words: *Hyperbilirubinemia, preterm, Sepsis*

Introduction

Jaundice is one of the commonest abnormal physical sign in the newborn[1]. It is observed during the first week of life in approximately 60% of the term & 80% of preterm infants[2]. Hyperbilirubinemia is defined as a total serum bilirubin level of >5mg/dL[2]. Neonatal hyperbilirubinemia is termed as significant when it needs close supervision, further evaluation and sometimes intervension[3,4]. In case of term baby, serum total bilirubin >17mg/dL beyond the age of 72 hours is termed as significant hyperbilirubinemia[3,5]. In case of preterm newborn significant hyper-bilirubinemia varies according to gestational age and birth weight[5,6]. Neonatal jaundice may not be a major cause of mortality but is an important cause of morbidity in the neonatal period and beyond [6]. The primary concern of hyperbilirubinemia is the neurotoxicity and cell injury that results from high

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levels of serum bilirubin. Prematurity is one of the risk factors for neonatal hyperbilirubinemia[2].

Neonatal jaundice is the most common reason for readmission after early hospital discharge[3,7]. 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[8]. This is not always possible in our country due to our limited facilities and economic constrains. The study was undertaken to know the pattern of serum total and indirect bilirubin levels in first two days of life from which significant hyperbilirubinemia may occur in the later part of first week of life. This will enable us to take right decision about the discharge of preterm babies from hospital in absence of other complicating factors and when feeding is established.

Methodlogy

The observational study was conducted in Dhaka Shishu (Children) Hospital from January to June, 2007. One hundred and eleven preterm newborn with gestational age of 30-37 weeks (210-258 days) were enrolled during their first day of life. Their gestational age was determined according to the first day of mother's last menstrual period and was additionally confirmed by the New Ballard Scoring system and antenatal Ultrasonographic examination or obstetric records. Newborns with gestational age of <30 weeks (d"209 days), 37 competed weeks (e"259 days) and with major congenital malformations were not included in the study. Babies were delivered by normal vaginal delivery and caesarian section. Newborns with severe perinatal asphyxia were excluded from the study.

During admission their Hb estimation, complete blood count & peripheral blood film, blood grouping with rhesus typing, serum bilirubin (total & indirect) were performed. Serum total and indirect bilirubin were repeated on the 2nd, 5th & lastly on the 7th day of life. The neonates were followed up upto 7 days of life. Phototherapy was given to them who developed hyperbilirubinemia following the guidelines for perinatal care by the American Academy of Pediatrics. Neonates who developed direct hyperbilirubinemia, Rh incompatibility, clinically or culture positive sepsis and who had evidence of hemolysis were excluded. Serum bilirubin was measured by using Colorimetric method in the Pathology Department of Dhaka Shishu Hospital. Serum total and indirect bilirubin values of day 1, 2 were statistically analyzed at different cut of points from which subsequent hyperbilirubinemia can develop on the later part of first week. Statistical data were analyzed with the descriptive analyses and the independent sample t and chi square tests by using SPSS (statistical package for social sciences) version 12 for Windows. Results were presented in tabulated form. P value of <0.05 was considered significant.

Results

The study population was all preterm newborn (30-37 weeks of gestation).They were divided into four groups according to their gestational age (Table-I). The maximum number was found in the 34-35 weeks (42.3%) gestational age. Among them 60 (54%) were male and 51 (46%) were female. Their birth weight ranges from 1050gm to 2500gm. The mean ± SD birth weight was 1754±341gm.

Table-I
Distribution of study population according to Gestational age (n=111)

Gestational age (wks)	No.	%
30-31	18	16.2
32-33	25	22.5
34-35	47	42.3
36-37	21	18.9
Mean ± SD	33.7	±2.0

Out of total 111 preterm, 38(34%) developed significant hyperbilirubinemia. Total 40 (36%) preterm had serum total bilirubin of <2 mg/dL on day 1. None of them developed significant hyperbilirubinemia during the first seven days of life (table II). Serum total bilirubin of <2 mg/dL on day 1 had 100% negative predictive value; sensitivity & specificity were 100% & 54.8% (Table III).

Table- II
Total serum bilirubin vs. subsequent hyperbilirubinemia

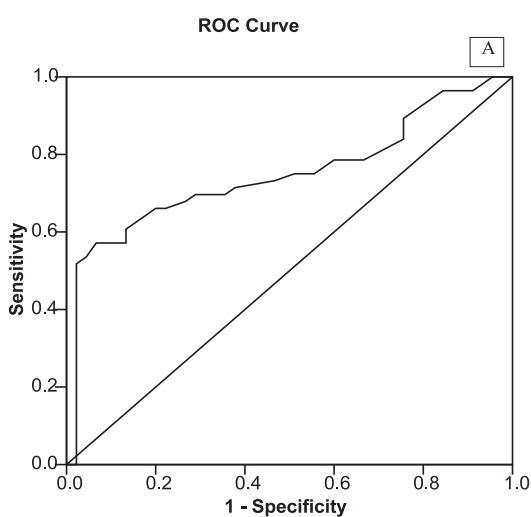| Total S bilirubin mg/dL	Total		Subsequent Hyperbilirubinemia	
	n	%	n	%
Day 1				
<2	40	36.0	nil	
2-3	27	24.3	7	25.9
3-5	25	22.5	13	48.0
>5	19	17.1	18	94.7
Day 2				
<5	65	58.5	5	7.6
5-7	23	20.7	14	60.9
s7-9	14	12.6	11	78.5
>9	9	8.1	8	88.8

Also total 65 (58.5%) preterm had serum total bilirubin of <5 mg/dL on day 2. Only 5 (7.6%) of them developed significant hyperbilirubinemia during the first seven days of life (table-II). So, on day 2, serum total bilirubin of <5 mg/dL had 92.3% negative predictive value (table III) ie. Only 7.6% chance to develop significant hyperbilirubinemia at this level of serum total bilirubin.

The risk for hyperbilirubinemia associated with day 1 serum total bilirubin values are at 5 mg/dL (OR= 64.8, 95% CI: 8.19-82.34) and at 3 mg/dL (OR= 14.14, 95% CI: 3.68-63.59).
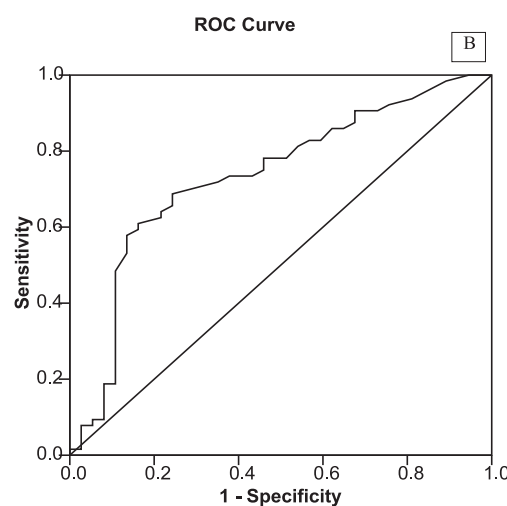
The risk for hyperbilirubinemia associated with day 2 serum total bilirubin values are at 9 mg/dL (OR=19.20, 95%CI: 2.26-27.34) and at 5 mg/dL (OR=30.46, 95% CI: 9.01-110.64). The area under ROC curve (C statistics) was 0.750 for day 1 and 0.733 for day 2.

Table -III
Predictive characteristics of day 1 and day 2 serum total bilirubin at different cut off points

S.Total bilirubin as risk demarcator	No of preterms (Total= 111)	Subsequent significant hyperbilirubinemia		Predictive Characteristics			
		Present	Absent	Sensitivity (%)	Specificity(%)	PPV (%)	NPV(%)
Day 1							
>5	19	18	1	47.4	98.6	94.7	78.3
<5	92	20	72				
>3	44	31	13	81.6	82.8	70.5	89.6
<3	67	7	60				
>2	71	38	33	100.0	54.8	53.5	100
<2	40	0	40				
Day 2							
>9	9	8	1	21.1	98.6	88.9	70.6
<9	102	30	72				
>7	23	19	4	50.0	94.5	82.6	78.4
<7	88	19	69				
>5	46	33	13	86.8	82.2	71.7	92.3
<5	65	5	60				

Receiver operating characteristic (ROC) curves with the discriminative performance of day 1 (A) and day 2 (B) serum total bilirubin for predicting subsequent hyperbilirubinemia.

Table IV
Area under the above curve

	C-statistics	Standard error	95% confidence interval	
Day 1 TSB	0.750	0.050	0.653	0.848
Day 2 TSB	0.733	0.053	0.629	0.838

TSB-Total serum bilirubin

Discussion

The practice of early postnatal discharge of neonates is a growing trend world wide. Such practice increases the risk of not detecting significant hyperbilirubinemia as discharge happens when serum bilirubin is still increasing[7,8]. Screening and early detection is therefore important to prevent bilirubin induced neurological dysfunction [9,10]. The present study was conducted to measure the risk of development of significant hyperbilirubinemia on the 5th and 7th days of life from the serum bilirubin values of the first and second day in preterm babies.

One prospective study by Maisels et al.[11] showed that near term (35-37 weeks gestation) newborns had higher serum total bilirubin levels on days 5 and 7 in comparison with term newborns (38-42 weeks gestation).

In our study the premature neonates also showed a rise of serum total bilirubin on 5th and 7th days. This later peak of serum bilirubin demonstrates the necessity of a relatively longer follow-up of these infants with respect to the development and duration of significant hyperbilirubinemia.

Out of total 111 preterms, 38(34%) developed significant hyperbilirubinemia within first seven days of life. Total 40(36%) preterms had serum total bilirubin of <2 mg/dL on day 1 (table-II). None of them developed significant hyperbilirubinemia during the first 7 days of life. So, serum total bilirubin of <2 mg/dL on day 1 had 100% negative predictive value. Also total 65(58.5%) preterms had serum total bilirubin of <5 mg/dL on day 2. Only 5(7.6%) of them developed significant hyperbilirubinemia during the first 7 days of life. So, on day 2, serum total bilirubin of <5 mg/dL had 92.3% negative predictive value ie. Only 7.7% chance to develop significant hyperbilirubinemia at this level of serum total bilirubin.

Again out of total population, 19(17.1%) had serum total bilirubin >5 mg/dL on day 1(table-II). Among them 18(94.7%) developed significant hyper-

bilirubinemia within first week. The positive predictive value was 94.7 and it was 98.6% specific (table III). The day 2 serum total bilirubin value was >9 mg/dL in case of 9 preterms. Out of them 8(88.8%) developed significant hyperbilirubinemia within first week. The positive predictive value was 88.9 and it was 98.6% specific (table III).

A similar kind of prospective study was done by Bhat et al. [5] over 461 healthy term neonates showed that, 29.3% babies had transcutaneous bilirubin index <5 at 24 hours and 43.3% had <8 at 48 hours. None of them had later significant hyperbilirubinemia (100% negative predictive value).

Significant hyperbilirubinemia has increased from 25.9% to 94.7% when day 1 serum total bilirubin value raised from <2 to >5 mg/dL and also from 60.9% to 88.8% when day 2 serum total bilirubin value rose from <5 to >9 mg/dL (table-II).

The risk for hyperbilirubinemia associated with day 1 serum total bilirubin values are at 5 mg/dL (OR= 64.8, 95% CI: 8.19-82.34) and at 3 mg/dL (OR= 14.14, 95% CI: 3.68-63.59). Similarly the risk for hyperbilirubinemia associated with day 2 serum total bilirubin values are at 9 mg/dL (OR= 19.20, 95% CI: 2.26-27.34) and at 5 mg/dL (OR= 30.46, 95% CI: 9.01-110.64). The area under curve (C statistics) was 0.750 for day 1 and 0.733 for day 2 (table IV). The C statistics for Bhat et al's [5] studies was 0.838 and 0.836 for 24 hour and 48 hour transcutaneous bilirubin index respectively indicating good predictive ability.

A study by Zakia et al.[12] done in our country over 84 healthy term and preterm newborns for predicting hyperbilirubinemia showed that 6% of their term infant and 35% of preterm infant developed significant hyperbilirubinemia. In our study 34% preterm newborn developed significant hyperbilirubinemia. In Zakia et al.'s [12] study the safe limit for umbilical cord blood serum total bilirubin was 2.5 mg/dL. In our study the safe limit for serum total bilirubin on day one is 2 mg/dL from which chance of significant hyperbilirubinemia is less.

Conclusion

Each preterm low birth weight neonate should be observed carefully for neonatal jaundice and should have pre discharge screening for serum total bilirubin. From this study it can be concluded that preterm neonates who have serum total bilirubin 2 mg/ dL or less on day one have less chance to develop significant hyperbilirubinemia within first week of life.

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