Research Article

Cord bilirubin as a predictor for development of hyperbilirubinemia in term neonates

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Abstract

Introduction: Hyperbilirubinemia is a common problem among term newborns. Cord bilirubin level has been found to correlate well with day 3 bilirubin level. We studied whether cord bilirubin could predict risk of development of significant hyperbilirubinemia among term neonates. **Methodology:** Prospective study from October 2009 -July 2010. All newborns between 37 weeks -42weeks, birth weight > 2500 gram, Apgar score > 7 at 1st& 5th minute of life were included in the study. Cord blood, day 3 & day 5 bilirubin was collected. Maternal data & bilirubin values were collected & analyzed using SPSS software. **Results:** About 115 babies were studied. There was no significant difference in cord bilirubin & day 3 bilirubin between babies born to mothers < 30 years &> 30 years. There was no significant difference in bilirubin values bassed on mode of delivery. About 29.6% babies developed clinical jaundice & received phototherapy. Cord bilirubin levels had significant association with need of phototherapy. Cord bilirubin >/= 2.1 mg/dl predicted need for phototherapy with PPV of 90.3%. Maternal age, sex of baby, birth weight & gestational age had no significant effect on cord bilirubin levels. Cord bilirubin >/= 2.1 mg/dl predicted day 3 serum bilirubin > 15 mg/dl with sensitivity of 88 % & PPV of 77.49 %. The likelihood ratio with cord bilirubin > 2.1 mg/dl & day 3 serum bilirubin > 15 mg/dl was 9.316. **Conclusion:** Cord bilirubin is predictive of need of phototherapy & correlated well with day 3 bilirubin levels which would facilitate early management of neonatal hyperbilirubinemia.

Keywords: Cord bilirubin, Neonatal hyperbilirubinemia, Phototherapy

Introduction

The commonest problem encountered during neonatal period among term neonates is Hyperbilirubinemia [1], which prolongs hospital stay in a majority of babies. Hyperbilirubinemia is defined as a serum total bilirubin concentration greater than 95th centile for hour of life. Common factors responsible for hyperbilirubinemia among term babies include increased bilirubin load due to relative polycythemia, shortened erythrocyte life span, immature hepatic intake & conjugation processes along with increased enterohepatic circulation. Uncontrolled hyperbilirubinemia leads to irreversible bilirubin toxicity which is often devastating leading to severe neurologic insult, chronic bilirubin encephalopathy, developmental & motor delays, sensorineural deafness & mild mental retardation. Recent practice of early discharge of term newborns places them at high risk for developing bilirubin encephalopathy [2,3,4]. Of late, Cord bilirubinlevel is being increasingly studied to define a subgroup of newborns that are at higher risk for developing significant hyperbilirubinemia. Hence this study was done to assess cord bilirubin as a predictor of neonatal hyperbilirubinemia.

Objective: To determine whether cord bilirubin level could predict risk of development of significant hyperbilirubinemia among term neonates.

Study design: Prospective study.

Study area: Neonatal unit of Pondicherry institute of medical sciences (PIMS).

Study period: October 2009– July 2010.

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Study population: Healthy term newborn babies who were born at the maternity unit of PIMS.

Inclusion criteria: All newborn babies with gestational age between 37 weeks & 42 weeks, birth weight > 2500 gram, Apgar score of at least 7 at the 1st& 5th minute of life were included in the study.

Exclusion criteria: Babies who were of preterm or post term gestation, birth weight < 2500 gram, Apgar score less than 7 at 5 minutes, Babies with major congenital malformations were excluded from the study.

Methodology

Parental consent was obtained. Under aseptic conditions umbilical cord blood of the newborn was collected at the time of delivery & serum bilirubin level was estimated by Jendrassik method in the biochemistry department on all days. All newborns were examined for clinical jaundice by the investigator & a paediatric consultant. If found icteric treatment was started according to protocol. On day 3 & day 5, serum bilirubin level was estimated.

Interventions: Phototherapy to icteric babies as per standard unit protocol.

Data Analysis: Data collected were enrolled in excel sheets & was analyzed using SPSS 17 version (Statistical Package for Social Science). A p-value of <0.05 was considered significant.

Results

About 115 babies were enrolled during the study period. 61 babies (53%) were male & 54 babies (47%) were female.

Table 1: Comparison of cord bilirubin with maternal age, weight & sex of the baby.

		Cord Bilirubin				
			0.5-1	1.1-2	2.1-3	3.1-4
Maternal Age	< 30 YEARS	Number	6	62	22	4
		%	5.2	53.9	19.1	3.5
	> 30 YEARS	Number	1	15	5	0
		%	0.9	13	4.3	0
Weight	AGA	Number	6	62	4	95
		%	6.2	53.9	3.5	82.6
	SGA	Number	0	11	3	0
		%	0	9.6	2.6	0
	LGA	Number	1	4	1	6
		%	0.9	3.5	0.9	5.2
Sex	MALE	Number	1	49	11	0
		%	0.9	42.6	9.6	0
	FEMALE	Number	6	28	16	4
		%	5.2	24.3	13.9	3.5

About 94 babies (81.7%) were born to mothers of age between 20-30 yrs. Analysing the bilirubin values based on maternal age, there was no statistically significant difference in the cord bilirubin level & day 5 bilirubin in babies born to mothers < 30 years of age when compared to mothers > 30 years of age. About 113 (98.3%) of the 115 mothers in the study group had no antenatal medical complication; 1 mother had gestational diabetes & 1 mother had hypertension. About 65 mothers (56.5%) delivered by spontaneous vaginal delivery & 49 mothers (42.6%) delivered by lower segment caesarian section.

Analysing the bilirubin values based on mode of delivery, there was no statistically significant difference in the bilirubin values in babies born by vaginal delivery as compared to babies born by section. About 95 babies (82.6%) were appropriate for gestational age. About 77 babies (67%) had cord blood bilirubin in the range of 1.1 – 2 mg/dl whereas 30 babies (27%) had cord blood bilirubin > 2.1 mg/dl. About 73 babies (63.5%) had day 3 serum bilirubin in the range of 10.1 - 15 mg/dl whereas 27 babies (23.5%) had day 3 serum bilirubin > 15 mg/dl.

Table 2: Cord bilirubin & need of phototherapy.

	Phototherapy			
			YES	**NO**
Cord Bilirubin	**0.5-1**	**Number**	1	6
		%	0.9	5.2
	1.1-2	**Number**	9	68
		%	7.8	59.1
	2.1-3	**Number**	24	9
		%	20.9	2.6
	>3.1	**Number**	4	0
		%	3.5	0

About 38 babies (29.6 %) developed clinical jaundice & received phototherapy. Cord bilirubin levels had statistically significant association with the need of phototherapy. Cord bilirubin > / = to 2.1 mg/dl predicted the need for phototherapy with positive predictive value of 90.3%. Maternal age, sex of the baby, birth weight & gestational age had no statistically significant effect on cord bilirubin levels.

Table 3: Correlation between cord bilirubin & day 3 serum bilirubin

	Day 3 Bilirubin					
			5.1-10	**10.1-15**	**15.1-20**	**>20**
Cord Bilirubin	**0.5-1**	**Number**	4	3	0	0
		%	3.5	2.6	0	0
	1.1-2	**Number**	10	64	2	1
		%	8.7	55.7	1.7	0.9
	2.1-3	**Number**	1	6	20	0
		%	0.9	5.2	17.4	0
	>3.1	**Number**	0	0	4	0
		%	0	0	3.5	0

Table 4: Cord bilirubin versus day 3 serum bilirubin- predictive value

		Total serum bilirubin day 3		**Sensitivity**	**Specificity**	**PPV**
		> 15	**<15**			
Cord Bilirubin Cut Off	**> 1.1**	**24**	**81**	100%	7.80%	22.80%
	< 1.1	**0**	**7**			
	>2.1	**24**	**7**	88%	91%	77.49%
	<2.1	**3**	**81**			
		>13	**<13**			
	>1.1	**57**	**54**	100%	100%	51.30%
	<1.1	**0**	**4**			
	<2.1	**38**	**10**	**66.60%**	**71.60%**	**79.10%**
	<2.1	**19**	**48**			
		>10	**<10**			
	>1.1	**67**	**10**	95.70%	57%	87%
	<1.1	**3**	**4**			
	<2.1	**30**	**1**	30%	16%	96.70%
	<2.1	**70**	**14**			

Table-5: Cord bilirubin versus day 3 bilirubin cut off likely hood ratio.

Day 3 Bilirubin											
			> 15	< 15	LR	> 13	< 13	LR	> 10	< 10	LR
Cord Bilirubin	0.5-1	Number	0	7	0	0	4	0	3	4	0.11
		%	0	7.95		0	7		3	26.6	
	1.1-2	Number	3	74	0.13	20	43	0.45	67	10	1
		%	11.1	84.09		34	75.4		67	66.6	
	2.1-3	Number	20	7	9.316	35	10	0.44	26	1	3.9
		%	74.07	7.95		60.3	17.5		26	6.6	
	>3.1	Number	4	0	14.81	3	0	0	4	4	0
		%	14.81	0		5.1	0		4	0	

In this study cord bilirubin > / = to 2.1 mg/dl predicted day 3 serum bilirubin level > 15 mg/dl with a sensitivity of 88 % & positive predictive value of 77.49 %. The likelihood ratio with cord bilirubin cut off > 2.1 mg/dl & day 3 serum bilirubin> 15 mg/dl was 9.316. Cord bilirubin > / = 1.1 mg/dl predicted day 3 serum bilirubin level > 15 mg/dl with a sensitivity of 100 % & positive predictive value of 22.8 %. The likelihood ratio with cord blood bilirubin cut off 1.1-2.0 mg/dl & day 3 serum bilirubin > 15 mg/dl was 0.13. Cord bilirubin > / = to 2.1 mg/dl predicted day 3 serum bilirubin level > 13 mg/dl with a sensitivity of 66.66 % & positive predictive value of 79.1 %. The likelihood ratio with cord blood bilirubin cut off > 2.1 mg/dl & day 3 serum bilirubin> 13 mg/dl was 3.44. Cord bilirubin > / = 1.1 mg/dl predicted day 3 serum bilirubin level > 15 mg/dl with a sensitivity of 100 % & positive predictive value of 51.3 %. The likelihood ratio with cord blood bilirubin cut off 1.1- 2.0 mg/dl & day 3 serum bilirubin > 15 mg/dl was 0.45. Cord bilirubin > / = to 2.1 mg/dl predicted day 3 serum bilirubin level > 10 mg/dl with a sensitivity of 30 % & positive predictive value of 96.7%. The likelihood ratio with cord blood bilirubin cut off > 2.1 mg/dl & day 3 serum bilirubin > 10 mg/dl was 3.9. Cord bilirubin > / = 1.1 mg/dl predicted day 3 serum bilirubin level > 15 mg/dl with a sensitivity of 95.7 % & positive predictive value of 87 %. The likelihood ratio with cord blood bilirubin cut off 1.1- 2.0 mg/dl & day 3 serum bilirubin > 10 mg/dl was 1.0.

Discussion

Reticulocyte count, positive direct antiglobulin test & presence of a sibling with neonatal jaundice have been considered as good predictors for the development of significant hyperbilirubinemia. Studies have shown that critical bilirubin levels of 4 mg/dl & 6 mg/dl at the 6th hour of life predicted occurrence of significant hyperbilirubinemia & development of severe haemolytic disease of the newborn, respectively [3,5]. There is an association between bilirubin levels in cord blood & later neonatal bilirubin concentration [6,7,8]. Mean bilirubin levels in cord blood range from 1.4 to 1.9 mg/dl [9,10] & elevated cord bilirubin levels was associated with an increased risk of hyperbilirubinemia [7,9,10]. Risenberg et al [11] observed that babies with cord bilirubin more than 4mg/100ml were at risk of developing severe hyperbilirubinemia. Rosenfeld et al., [12] concluded that babies with cord bilirubin level < 2mg/dl had 4% chance of developing significant jaundice as compared to a 25% chance of developing significant jaundice in newborns with level > 2mg/dl. Knudson A [6] noted that need of phototherapy was statistically significant among newborns with cord bilirubin levels > 2.3 mg/dl as compared to babies with bilirubin < 2.3 mg/dl. Mathias Katfer et al.,[13] observed that newborns with cord bilirubin > 30 micromol/ litre predicted need of phototherapy with a sensitivity of 90 % & a negative predictive value of 99.1 %. Serum cord total bilirubin levels can define a subgroup of infants who are at a higher risk for developing significant hyperbilirubinemia& requirement of phototherapy. Yamauchi Y et al., [7] observed that babies delivered by caesarean section had significant lower values of cord bilirubin as compared to babies delivered vaginally which was explained due to decreased placental transfusion during caesarean section. In our study there was no significant difference based on the mode of delivery. Srivastsav N et al., [14] in his study comparing newborns born to mothers with age < 30 years and mothers > 30 years found that babies born to younger mothers had higher bilirubin on day 3 & day 5. However no statistically significant difference was observed on cord bilirubin. In our study there was no statistically significant difference in the cord bilirubin level & day 5 bilirubin in babies born to mothers < 30 years of age as compared to mothers >30 years of age.

Conclusion

Umbilical cord bilirubin is useful in predicting the postnatal bilirubin value on day 3 & need for phototherapy in normal term newborns. Cord bilirubin cut off of > / = 2.1 mg/dl among term neonates is a good predictor of total serum bilirubin > 15 mg/dl with good sensitivity & positive predictive value which would facilitate targeted intervention of babies at high risk of hyperbilirubinaemia in a safe & cost effective manner.

Recommendations: Umbilical cord blood bilirubin of term newborn babies would facilitate early intervention in the management of neonatalhyperbilirubinemia thereby reducing hospital stay in a resource limited country like ours.

Abbreviations:
CB- cord bilirubin
TSB- total serum bilirubin
PPV- positive predictive value
LR- likelihood ratio
PT- phototherapy

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