To Study the Predictive Value of Umbilical Cord Bilirubin in Neonatal Hyperbilirubinemia

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ABSTRACT

Introduction: Jaundice is a clinical condition that is often present in pediatric practice and constitutes one of the major issues within the neonatal period. It occurs in both the physiological and pathological processes in newborns. Study aimed to evaluate the predictive value of umbilical cord bilirubin in identifying term newborns with ABO/Rh incompatibility for subsequent hyperbilirubinemia in 1st week of life.

Material and Methods: 150 Term newborns with the gestational age of 36-40 weeks with the APGAR score of over 7 at the first minute and 10 at the fifth minute of life were taken. Baby with significant illness or major congenital malformation were excluded from the study.

Results: 150 newborns were divided into hyperbilirubinemia and non- hyperbilirubinemia groups. Mean total Cord Bilirubin is more in Rh incompatibility (4.23) when compared to ABO incompatibility (3.86). Mother's blood group has statistical signification with Hyperbilirubinemia and Non-hyperbilirubinemia, but it was not seen in the baby's blood group. The mean Hb of Hyperbilirubinemia and Non-hyperbilirubinemia is 15.6 ± 0.7 and 14.2 ± 2 gm/dL respectively, and the difference between them was statistically significant. The mean Cord Bilirubin between babies with Hyperbilirubinemia and Non-hyperbilirubinemia was 4 ± 0.5 and 2.3 ± 0.3 mg/dL respectively, and the difference between them was statistically significant. The relationship between total Cord Bilirubin and SBR was statistically significant

Conclusion: The total cord bilirubin in healthy term newborns provides the prediction for neonatal jaundice in 1st week of life. The cut-off value is 3.25 with 96% of specificity and 96% sensitivity.

Keywords: Hyperbilirubinemia, Neonate, Prediction, Prevention, Umbilical Cord Blood

INTRODUCTION

Babies are called newborns during their first month of life. After birth, mostly we can witness that babies sleep a lot this is because of a lot of changes that takes place inside their body system. Mostly about 85% of term newborns and premature infants develop jaundice. There are various clinically proven reason for this. In this thesis, we are mainly focused on Cord Bilirubin and its significance in predicting neonatal jaundice. Most babies have mild jaundice. It usually gets better or goes away on its own within a week or two without causing problems. Generally, jaundice should be taken seriously; it may be physiological or pathological. In rare cases, if the bilirubin level stays high and isn't treated, it can cause brain damage called kernicterus (This term was introduced in early 1900s, it refers to the yellow staining

of basal ganglia that was noticed in newborns died with severe jaundice). This can lead to serious life problems too. At times this condition becomes life-threatening if it's not properly taken care which may lead to hyperbilirubinemia. We are mainly concerned about the various cause, ill effects as well the prevention mechanism of it.[1-3]

Jaundice a most common condition that requires medical attention. In order to develop a diagnostic as well management of jaundice in newborns, we need to have a clear background idea about pathological and non-pathological factors as well as their bilirubin levels. Approximately 60-65% of term infants and 80-85% of preterm infants develop jaundice. About 10% of breastfed babies still have been identified with jaundice within 1 month of age. Various risk factors that are responsible are birth weight less than 2500gms or premature infants, if previous siblings TSB≥12 mg/dL subsequent sibling is prone to jaundice, newborns of mother who have diabetes section, male child have been reported more compared to females, people living at higher altitude, East Asian babies have increased bilirubin compared to others and neonatal infection adds risk to hyperbilirubinemia.[4-7]

Study aimed to evaluate the predictive value of umbilical cord bilirubin in identifying term newborns with ABO/Rh incompatibility for subsequent hyperbilirubinemia in 1st week of life.

MATERIAL AND METHODS

The prospective clinical study was done in Tirunelveli Medical College Hospital (TVMCH) which is carried out in all consecutive term newborns with ABO/Rh incompatibility over a period of 8 months duration. The study population was initially followed up clinically by Kramer's method and by transcutaneous bilirubinometer. Newborns identified with jaundice were followed up using serial serum bilirubin values.

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Inclusion criteria

All consequently born babies in Tirunelveli Medical College Hospital irrespective to the mode of delivery and gender were included. Term newborns with the gestational age of 36-40 weeks were included. APGAR score of over 7 at the first minute and 10 at the fifth minute of life is taken. The absence of significant illness or major congenital malformation is the another inclusion criteria.

Exclusion criteria

Term newborns with the significant illness like sepsis, respiratory distress syndrome, infant of the diabetic mother, asphyxia that could aggravate hyperbilirubinemia. Low birth weight newborns ($\leq$ 2kg).

Total serum bilirubin, conjugated bilirubin, unconjugated bilirubin were obtained via the calorimetric diazo method.

RESULTS

The study subjects of 150 newborn babies were observed for 1 week, and those who have developed hyperbilirubinemia and they were classified as, and the remaining babies were treated as ordinary babies. The various analysis and

Mothers' age group	Non-hyper bilirubinemia		Hyper-bilirubinemia		Total	
	Frequency	%	Frequency	%	Frequency	%
20-24	11	22	26	26	37	24.7
25-29	38	76	42	42	80	53.3
30-34	1	2	27	27	28	18.7
35-39	0	0	5	5	5	3.3
Total	50	100	100	100	150	100
Mean ±SD	25.9±2.1		27.2±4.1			
Significance	P<0.05					

Table-1: Age of mothers compared between the Hyperbilirubinemia and Non-hyperbilirubinemia

Blood group	Non-hyper bilirubinemia		Hyper-bilirubinemia		Total		X²	d f	significance
	No	%	No	%	No	%			
A-	1	2	9	9	10	6.7			
A+	17	34	3	3	20	13.3			
AB+	4	8	8	8	12	8			
B-	0	0	11	11	11	7.3	37.711	6	P<0.001
B+	12	24	15	15	27	18			
O-	2	4	13	13	15	10			
O+	14	28	41	41	55	36.7			
Total	50	100	100	100	150	100			

Table-2: Mothers' blood group associated with incidence of Hyperbilirubinemia and Non-hyperbilirubinemia

ABO incompatibility	Non-hyper bilirubinemia		Hyper-bilirubinemia		Total		significance
	No	%	No	%	No	%	
Nil	40	80	64	64	104	69.3	
Yes	10	20	36	35	46	30.7	P<0.05
Total	50	100	100	100	150	100	

Table-3: The association between the ABO incompatibility with Non-hyperbilirubinemia and Hyperbilirubinemia

Rh incompatibility	Non-hyper bilirubinemia		Hyper-bilirubinemia		Total		Significance
	No	%	No	%	No	%	
Nil	50	100	73	73	123	82	P<0.001
Yes	0	0	27	27	27	18	
Total	50	100	100	100	150	100	

Table-4: The association between the Rh incompatibility with Non-hyperbilirubinemia and Hyperbilirubinemia

Variable	Non-hyper bilirubinemia=50		Hyper bilirubinemia=100		significance
	Mean	SD	Mean	SD	
GA	36.5	0.5	36.6	0.5	P>0.05
BW	2.6	0.3	2.7	0.3	P>0.05
Hb	14.2	2.1	15.6	0.7	P<0.001
Apgar 1m	7.2	0.4	7.1	0.3	P>0.05
Apgar 5m	8.16	0.4	8.18	0.4	P>0.05

Table-5: Comparison of perinatal characteristics between Non-hyperbilirubinemia and Hyperbilirubinemia

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Total	Non-hyper bilirubinemia=50		Hyper bilirubinemia=100		significance
	Mean	SD	Mean	SD	
CORD bilirubin	2.3	0.3	4	0.5	P<0.001
SBR	2.6	0.4	8.8	2.6	P<0.001

Table-6: Comparison of total cord bilirubin and SBR between Non-hyperbilirubinemia and Hyperbilirubinemia at birth

Variable	B	SE	Wald	df	P	EXP (B)
GA	2.609	1.919	1.849	1	0.14	13.587
Sex (M)	3.217	5.367	0.359	1	0.549	24.949
ABO	-2.149	1.788	1.444	1	0.229	4.117
Rh	-19.122	5191.355	0	1	.093	0
CORD bilirubin total	11.447	4.342	6.949	1	.008	93591.7
Constant	-126.134	76.972	2.685	1	.101	.000

Table-7: Logistic regression on GA, SEX, ABO, Rh and Cord Bilirubin total

Cord Bilirubin Level	Hyperbilirubinemia	Non-hyperbilirubinemia	Sensitivity	Specificity	PPV	NPV	Youden index
≥3.25	99	2	96.0%	96.0%	98	97.9	0.959
<3.25	1	48					
Total	100	50					

Table-8: Predictive value of Hyperbilirubinemia

Pair	Pre		Post		Difference		P value
	Mean	SD	Mean	SD	Mean	SD	
12th to 24th	12.1	9.0	10.2	1.1	1.9	9.1	P<0.05
24th hour to phototherapy	10.2	1.1	8.4	1.3	1.8	0.7	P<0.001
12th hour to phototherapy	12.1	9.0	8.4	1.3	3.7	9.1	P<0.001

Table-9: Comparison of Hyperbilirubinemia from 12th to 24th hour, 24th hour to Phototherapy transfusion and 12th hour to Photo-therapy transfusion

Rh	Phototherapy transfusion						Significance
	No	%	Yes	%	Total	%	
No	122	88.4	1	8.3	123	82	P<0.001
Yes	16	11.6	11	91.7	27	18	
Total	138	100	12	100	150	100	

Table-10: Association between Rh incompatibilities with Phototherapy transfusion

interpretations were made by comparing the two groups. The groups were described according to their mother's age, Gestational age, parity mode of delivery mother's blood group and the neonate's blood group.

The mean age Non-hyper bilirubinemia neonatal mothers were 25.9±2.1 years. The mean age of hyperbilirubinemia neonatal mothers was 27.1±4.1 years. The difference between the above means was statistically significant, (P<0.05).

The results revealed that the primipara neonates were associated with Non-hyperbilirubinemia and the multipara neonates were associated with Hyperbilirubinemia. The relationship was statistically very highly significant (p<0.001). (Table 1)

The mothers' blood groups A-, B-, O- and O+ were associated with Hyperbilirubinemia neonates and A+ and B+ were associated with Non hyperbilirubinemia. The associations were statistically very highly significant (P<0.001) (Table 2). The neonates blood groups were not significantly associated with Non hyperbilirubinemia and Hyperbilirubinemia (P>0.05).

The ABO incompatibility shown in the above table had associated with the Hyperbilirubinemia (35%) and not associated with Non hyperbilirubinemia (80%). These associates were statistically significant (P<0.05) (Table 3).

The Rh incompatibility shown in the above table had associated with the Hyperbilirubinemia (27%) and nil associated with Non hyperbilirubinemia (100%). These associations were statistically very highly significant (P<0.05) (table-4).

The perinatal characteristics of neonatal such as gestational age, birth weight, Hb. Apgar scores 1mt and 5mts were compared between Non-hyperbilirubinemia and Hyperbilirubinemia.

The variables except Hb, the others did not differed significantly. The mean Hb of Non hyperbilirubinemia was 14.2±2.1gms/dl and the same of Hyperbilirubinemia was 15.6±0.7gms/dl. The difference between them was statistically very highly significant (P<0.001) (Table 5).

The mean cord bilirubin total of two groups was 2.3±0.3 and 4.0±0.5. The difference was statistically significant

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(P<0.001). Similarly the mean difference between them was statistically very highly significant (P<0.001).

The relationship between total cord bilirubin and SBR was statistically very highly significant (P<0.001). (Table 6)

The variables such as cord bilirubin total, gestational age, gender, ABO incompatibility and Rh incompatibility were inter related variables in predicting the cut point of cord bilirubin total. The logistic regression results are tabulated in table 7.

In the table -7 except Cord Bilirubin total all variable are not statistically significant (P>0.05). Hence the logistic regression was applied only for Cord Bilirubin total with Non-hyperbilirubinemia and Hyperbilirubinemia.

The curve estimation was done statistically significant (P<0.001). The diagonal segment would give the predictive value of cord bilirubin total for hyperbilirubinemia. (Figure 1)

The table 8 states the cut off value is 3.25 of cord bilirubin total. At this point the sensitivity is 96.0% and specificity is 96.0% and the Youden index is highest (0.959).

The SBR total of Non hyperbilirubinemia was statistically significantly lesser than the other days. Similarly, the 1st day Hyperbilirubinemia total SBR was significantly greater than the other days. The other three days total SBR were significantly lesser than the 1st day.

The reduction of reduction of total SBR with in the hyperbilirubinemia were statistically significant (Table 9).

The table 10 shows the association between Rh incompatibilities with phototherapy transfusion. The results revealed that the phototherapy transfusion very strongly associated with Rh incompatibilities (P<0.001).

DISCUSSION

Neonatal hyperbilirubinemia is one of the most common clinical entity that we come across with newborns. Mostly 85% of term and preterm newborns develop jaundice. Prediction of neonatal jaundice is more important as severe jaundice (Kernicterus) can occur in a healthy term baby with no clinically apparent jaundice in 24 hours. In this study, we have arrived in a predictive value of cord bilirubin for neonatal jaundice in 1st week of life.

Our study population contains 150 newborns in which 100 newborns developed jaundiced, and 50 newborns have no jaundice. Out which 37.3% were the male baby, and 62.7% were the female baby. In this study, we found that hyperbilirubinemia did not have any significant association with the gender of the baby (P value of more than 0.05). In one study among preterm group, mean cord bilirubin was significant in males compared to female babies. In full-term group, mean cord bilirubin among male and female babies have no statistical significance.[8,9]

In this study, the mean gestational age is 36.5±1wks and found this variable did not differ significantly. Mathias et al. found that mean cord bilirubin is negatively correlated with gestational age.[10]

In this study, the mean birth weight is 26±0.1 was found that this variable did not differ significantly (P value more than

0.05).

Adelia et al. found that there was no significant correlation between total cord bilirubin and birth weight (≥ 3.5kg). Preterm and low birth weight newborns are more likely to develop jaundice as the liver is immature with low UDPGT with decreased liver excretion.[11]

In this study mode of delivery was 40% labour natural and 60% was caesarean section. Test of significance state that P more than 0.05, i.e., there was no statistical significance between cord bilirubin and mode of delivery. These results matched with Amar et al and Rostami et al.[8,9]

In this study, ABO incompatibility requiring phototherapy is present in 30%, and non-ABO constitutes 69.3% showed that there was no statistically significant association between ABO incompatibility and phototherapy (P more than 0.05). In one study mean cord bilirubin for newborns who had phototherapy was 2.19±0.24 mg/dL which is highly significant than those who didn't receive it (1.49 ± 0.34 mg/dL). This study matched with Adelia et al.[11]

In this study, about 18% of newborns with Rh incompatibility underwent phototherapy whereas 82% of newborns without Rh incompatibility underwent phototherapy. The p-value less than 0.001 indicates that phototherapy is very strongly associated with Rh incompatibility.

In this study, the mean cord bilirubin was significantly higher among ABO +ve newborns compared to ABO –ve ones. The mean cord bilirubin is found to be greater in Rh than in ABO incompatible groups. These results didn't agree with Adelia et al. which showed that there is no significant difference in cord bilirubin between newborns with and without blood group incompatibility.[11]

In this study, the mean age of mother and newborn with no hyperbilirubinemia is 25.9±2.1 years, whereas on the other hand with hyperbilirubinemia is 27.2±4.1 years. The difference between the above mean was statistically significant with P less than 0.05.

In this study the mother with blood groups A-ve, B-ve, O-ve, O+ve were associated with hyperbilirubinemia and A+ve, B+ve were not statistically associated with hyperbilirubinemia (P value less than 0.001). Neonatal blood groups were not statistically significantly associated with hyperbilirubinemia and Non-hyperbilirubinemia.

In this study mean Hb of Non-hyperbilirubinemia was 14.2±2.1 gm/dL and hyperbilirubinemia was 15.6±0.7 gm/dL. The difference between them showed a very high statistical significance.

In this study mean cord bilirubin between newborns with Non-hyperbilirubinemia and hyperbilirubinemia were 2.3±0.3 and 4.0±0.5 respectively. The difference they proved statistical significance (P value less than 0.001).

In this study, the relation between total cord bilirubin and SBR were statistically highly significant. Logistic regression was applied only for cord bilirubin with Non-hyperbilirubinemia and hyperbilirubinemia because all other variables like GA, Sex, and incompatibility were not statistically significant.

In this study cord bilirubin cut off point calculated by ROC curve. The diagonal segment of this curve gives the

predictive value of cord bilirubin as 3.25 mg/dL. At this point, sensitivity and specificity was 96% with the youden index being 0.959 (Highest).

Rudy et al. determined this value using ROC as 2.54 mg/dL having high sensitivity and specificity. Amar et al. value was more than 2 mg/dL which had the highest specificity, and this critical bilirubin level had a very high NPV and fairly low PPV. Rostami et al. value more than 3 mg/dL states that it was not a useful predictor for jaundice.[8,9,12]

CONCLUSION

The study concludes that the total cord bilirubin in healthy term newborns provides the prediction for neonatal jaundice in 1st week of life. The cut-off value is 3.25 with 96% of specificity and 96% sensitivity. It is also evident that the presence of incompatibility in newborns (ABO, Rh) was statistically significant for the occurrence of high total cord bilirubin that indicates phototherapy treatment.

REFERENCES

1. American Academy of Paediatrics, Subcommittee on Neonatal Hyperbilirubinemia. Neonatal jaundice and kernicterus. Paediatrics. 2001;108:763–5.
2. American Academy of Paediatrics, Jaundice section of Infant nutrition and development of gastrointestinal function. In RE Kleinman, ed., Paediatric Nutrition Handbook, 6th ed., 2009; 47-49.
3. Kamath BD, Jaundice. In SL Gardner et al., eds., Merenstein and Gardner's Handbook of Neonatal Intensive Care, 7th ed., 2011; 531–552.
4. Sarci S U, Serdar MA, Korkmaz A, et al. Incidence, course and prediction of hyperbilirubinemia in near term and term newborns. Paediatrics. 2004;113: 775–780.
5. Kawade N, Onishi S. The perinatal and postnatal development of UDPglucuronyl transferase activity towards bilirubin and the effect of premature birth on its activity in human liver. Biochem J. 1981;196: 257–260.
6. Bhutani VK, Johnson LH, Maisels MJ et al. Kernicterus; epidemiological strategies for its prevention through system based approach. J Perinatol.2004; 24: 650–662.
7. Newman TB, Escobar GJ, Gonzales VM, Armstrong MA, et al. Frequency of neonatal bilirubin testing and hyperbilirubinemia in a large health maintenance organisation. Paediatrics 1999; 101: 995–998.
8. Amar. Taksande, Krishna. Vihekar, Manish, et al.Prediction of the development of neonatal hyperbilirubinemia by increased umbilical cord blood bilirubin. Indmedica Curr Pediatr Res, 2005;9:1-9.
9. N. Rostami, Y. Mehrabi. Identifying the newborns at risk for developing significant hyperbilirubinemia by measuring cord bilirubin levels. J Arab Neonatol Forum 2005;2:81-85.
10. K. Matthias, P. Ferdinand, G. Corinna, et al.Predictive value of umbilical cord blood bilirubin for postnatal hyperbilirubinemia. Acta Paediatr 2007;94:581-587.
11. Adelia Bernaldo, Canceicao SegreBilirubin dosage in cord blood: could it predict neonatal hyperbilirubinemia? Sao Paulo Med 2004;122: 5-19.
12. Rudy Satrya, Sjarif H. Effendi, Dida A. GurnidaCorrelation between cord blood bilirubin level and incidence of hyperbilirubinemia in term newborns. Paediatr Indones 2009;6:349-354.