

UMBILICAL CORD BILIRUBIN LEVEL AS A PREDICTOR OF SUBSEQUENT NEONATAL HYPERBILIRUBINAEMIA IN TERM HEALTHY NEWBORNS

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ABSTRACT

BACKGROUND

Hospital readmission due to neonatal hyperbilirubinaemia is a cause for concern among parents as well as clinicians. Early discharge carries the risk of delayed recognition of hyperbilirubinaemia and the possibility of bilirubin-induced brain damage.

The aim of the study is to correlate the umbilical cord bilirubin level as a predictor of subsequent neonatal hyperbilirubinaemia in term healthy newborns.

MATERIALS AND METHODS

This was a prospective study conducted at tertiary care teaching hospital for the period of one year. A total of 192 healthy term newborns were included in the study and subjected to cord blood analysis for bilirubin. Further at 72 hours of life, blood for serum bilirubin was again collected and the two values were compared.

RESULTS

Out of 192 neonates studied, 29 (15.1%) newborns were developed significant jaundice (serum bilirubin ≥ 17 mg/dL) at 72 hours of life. Term healthy newborns having cord bilirubin value < 2 mg/dL had only 2.8% risk of developing significant hyperbilirubinaemia when compared to newborns with cord bilirubin > 2.5 mg/dL who had 68.2% risk of developing hyperbilirubinaemia, which was statistically significant ($p < 0.005$). The cord bilirubin level of > 2.5 mg/dL had the higher specificity (95.7%), negative predictive value (91.8%) and fairly better positive predictive value (68.2%) in predicting significant hyperbilirubinaemia of ≥ 17 mg/dL at 72 hours of life.

CONCLUSION

Estimating cord blood bilirubin is helpful in identifying neonates who may develop significant hyperbilirubinaemia warranting therapeutic intervention. Increase in cord bilirubin level associated with increase in chances for subsequent hyperbilirubinaemia.

KEYWORDS

Cord Bilirubin, Hyperbilirubinaemia, Neonatal Jaundice, Healthy Newborn.

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BACKGROUND

Hyperbilirubinaemia is a common problem in neonates. About 60% of term infants and 80% of preterm infants suffer from jaundice.¹ It is also a cause for concern both for the parents as well as paediatricians. Severe hyperbilirubinaemia may lead to irreversible brain damage in otherwise healthy newborn. This can be easily prevented if excessive jaundice for the age is promptly identified and appropriately treated.

Recently, there is an increasing trend in early discharge of healthy term newborns within 48 hours. It can help in

reducing hospital stay, thereby reducing economic burden on parents. However, early discharge can lead to readmission and bilirubin-induced brain damage of these neonates due to late detection of hyperbilirubinaemia.² So, there is a need for development of a test, which can predict and thereby prevent a potential problem of hyperbilirubinaemia before it occurs.

Though, there are studies from western countries where they have utilised umbilical cord blood to assess the risk of subsequent hyperbilirubinaemia studies from India are limited.^{3,4} Therefore, this study was carried out to evaluate the cord bilirubin as an early predictor of significant neonatal hyperbilirubinaemia in a term infant.

MATERIALS AND METHODS

This study was conducted in a tertiary care teaching hospital. This was a prospective observational study from June 2013 to June 2014 for the period of one year. Study was carried out after obtaining prior approval from the

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institutional ethical committee. An informed consent was taken from parents.

Inclusion Criteria

All inborn full-term healthy neonates.

Exclusion Criteria-

1. Newborn babies with ABO/Rh incompatibility.
2. Sick neonates requiring NICU admission.
3. Presence of major congenital malformations and cephalohaematoma.
4. Neonates discharged prior to 72 hours of birth.

Thus, a total of 192 newborns were included in the study. Detailed history and examination including maternal history with special emphasis to known risk factors associated with hyperbilirubinaemia were carried out. About 3 mL of cord blood was collected and serum bilirubin level was estimated by colorimetric diazo method. All neonates were followed up clinically for the development of jaundice. Serum bilirubin was done in all the newborns at 72 hours. Umbilical Cord Bilirubin (UCB) was compared with serum bilirubin done at 72 hours. Neonates with serum bilirubin levels ≥ 17 mg/dL after 72 hours of life were defined as having significant hyperbilirubinaemia.^{5,6} Phototherapy was started, neonates with significant hyperbilirubinaemia and serum bilirubin levels are monitored more frequently if required.

The data analysis was done by using the SPSS version 17 and MS excel sheet. Sensitivity, specificity, negative and positive predictive values of different cut-off of cord bilirubin value was calculated. Relationships between variables were analysed by using Chi-square test and independent sample t-test. The p value of <0.05 was considered statistically significant.

RESULTS

During one year of study period, a total number of 192 newborns were included in the final analysis. Table 1 shows the incidence of hyperbilirubinaemia in healthy term neonates at 72 hours of life.

Bilirubin Range (mg/dL)	Total Number of Babies	Percentage
<5	2	1.0
5-9.9	58	30.2
10-16.9	103	53.7
17-19.9	26	13.5
≥ 20	3	1.6
Total	192	100

Table 1. Serum Bilirubin Level at 72 Hours

Out of 192 neonates studied, 29 (15.1%) newborns were developed significant jaundice (serum bilirubin ≥ 17 mg/dL) at 72 hours of life. Thus, majority of them had bilirubin <17 mg/dL. The mean bilirubin level was 12.2 ± 0.83 mg/dL with range of 3.8-22.1 mg/dL.

Table 2 and 3 are showing baseline characteristics of mother and babies.

Characteristics	Number of Babies with Significant Jaundice at 72 Hours	Total Number of Babies	%
Vaginal delivery	17	130	13.1
Caesarean section	12	62	19.4
Primigravida	13	83	15.7
Multigravida	16	109	14.8
No GDM*	23	160	14.4
With GDM	6	32	18.8
No PIH*	21	148	14.2
With PIH	8	44	18.2
No BOH*	26	173	15.0
With BOH	3	19	15.9
No oxytocin use	13	108	12.0
With oxytocin use	16	84	19.1
No ROM* >18 hours	18	126	14.3
ROM >18 hours	11	66	16.7

Table 2. Population Characteristics of Mother

*GDM- Gestational diabetes mellitus, PIH- Pregnancy-induced hypertension, BOH- Bad obstetrics history, ROM- Rupture of Membrane.

There was slightly higher incidence of jaundice noticed in newborns following caesarean section, oxytocin use and infant of diabetic mother. However, this was not statistically significant ($p>0.05$). Hyperbilirubinaemia following the caesarean section maybe due to haemoconcentration associated with inadequate feeding.

Characteristics	Number of Babies with Significant Jaundice at 72 Hrs.	Total Number of Babies	%
Sex	Male	14	14.9
	Female	15	15.3
Birth weight (gm)	<2500	9	20.5
	2500-4000	18	12.6
	>4000	2	40.0
Weeks of gestation	37-38	10	15.6
	39-40	15	13.9
	41-42	4	20
Blood group	O	10	14.7
	A	9	15.9
	B	8	16.7
	AB	2	11.1

Table 3. Population Characteristics of Newborns

There was no significant difference in occurrence of jaundice among male and female newborns. Mean birth weight of babies who had significant jaundice was 3.13 kg with standard deviation of ± 0.432 and for those babies who were not had jaundice was 2.99 ± 0.454 kg. Slightly higher incidence of jaundice was observed in low birth weight and large for gestational age babies. In babies with significant jaundice, the mean cord haematocrit was 44.21 ± 2.67 ,

which was not significantly different ($p > 0.05$) from babies who not had hyperbilirubinaemia (44.16 ± 1.74).

Table 4 suggests that term healthy newborns having cord bilirubin value < 2 mg/dL had only 2.8% risk of developing significant hyperbilirubinaemia when compared to newborns with cord bilirubin > 2.5 mg/dL who had 68.2% risk of developing hyperbilirubinaemia, which was statistically significant ($p < 0.005$).

Umbilical Cord Bilirubin (mg/mL)	Number of Babies with Significant Jaundice	Total Number of Babies	%
< 2	2	72	2.8
2 to 2.5	12	98	12.2
> 2.5	15	22	68.2
Total	29	192	

Table 4. Occurrence of Jaundice with Umbilical Cord Bilirubin Level

Those babies not having significant jaundice, the mean cord bilirubin was 1.95 ± 0.33 mg/dL, and those having significant jaundice, the mean cord bilirubin was 2.69 ± 0.34 mg/dL, which was statistically significant ($p < 0.05$). The overall mean cord bilirubin was 2.32 ± 0.35 and the range 1.1-3.9 mg/dL. Out of 120 babies whose cord bilirubin level between 2 to 3.9 mg/dL, 27 (22.5%) babies had developed significant hyperbilirubinaemia.

The values characterising the predictive ability of cord blood as a predictor for subsequent hyperbilirubinaemia are shown in Table 5. There was higher specificity and fairly better positive predictive value using cord bilirubin cut-off value of > 2.5 mg/dL when compared with value of ≥ 2 mg/dL in predicting subsequent hyperbilirubinaemia at 72 hours of life.

Umbilical Cord Bilirubin (mg/mL)	Sensitivity% (95%, CI)	Specificity% (95%, CI)	PPV*% (95%, CI)	NPV*% (95%, CI)
≥ 2	93.1 (77.2-99.2)	42.9 (35.2-50.9)	22.5 (19.7-25.5)	97.2 (90.1-99.3)
> 2.5	51.7 (32.5-70.6)	95.7 (91.4-98.3)	68.2 (48.9-82.8)	91.8 (88.4-94.2)

Table 5. Predictive Ability of Significant Jaundice Using Umbilical Cord Bilirubin

*PPV- Positive predictive value, NPV- Negative predictive value.

DISCUSSION

Jaundice in newborn is a very common problem. It occurs in both the physiological and pathological form. When the newborn stays at the hospital for 72 hours post delivery period, it is possible to observe the peaking of the physiological jaundice, thus allowing medical intervention, if necessary. However, the growing practice of early discharge of newborns has resulted in increase in readmission and re-emergence of bilirubin-related neurological sequelae.

The American Academy of Paediatrics (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.⁷ In developing countries like India, this recommendation is not practical due to limited follow up facilities. Therefore, it is important to establish safe marker to predict, especially for those at risk of developing significant hyperbilirubinaemia.

As early as 1986, Rosenfeld J mentioned about serum cord total bilirubin levels, which can define a subgroup of infants who are at a higher risk for developing significant hyperbilirubinaemia and requiring phototherapy.³ Infants with cord bilirubin levels less than 2.0 mg/dL have only a 4% chance of developing hyperbilirubinaemia and a 1.4% chance of needing phototherapy. However, if serum cord bilirubin levels are more than 2.0 mg/dL, the infant has a 25% chance of developing subsequent hyperbilirubinaemia. He concluded that with early discharge from the nursery, a

more common practice, this level can identify at an early age, those infants who need closer followup.

Rataj and his colleague reported that if cord bilirubin was less than 1 mg%, jaundice occurred in 2.4% newborns, whereas 89% of the infants with cord bilirubin above 2.5 mg% became jaundiced.⁸ Rudy Satra et al reported high sensitivity (90.5%) and specificity 85% using cord bilirubin cut-off of ≥ 2.54 mg/dL. However, they had considered serum bilirubin ≥ 12.9 mg/dL as a cut-off for significant neonatal hyperbilirubinaemia.⁹ A study conducted by Pabbati et al from India shows cord bilirubin level > 1.89 mg/dL had the highest sensitivity (96.36%), very high negative predictive value (99.45%) and fairly low (26.4%) positive predictive value.¹⁰ In another Indian study by Ahire N et al reported sensitivity of 100%, specificity of 98.17% and positive predictive value of 66.67%, negative predictive value of 100% using cord bilirubin cut-off ≥ 3 mg/dL.¹¹

Thus, it can be seen that different authors have used different cut-off value for predicting significant jaundice. Bilirubin estimation varies from laboratory to laboratory, depends on methods used, technical error, ethnic makeup of people, etc. Therefore, it is better to have local laboratory cut-off value that can be used as a predictor for development of significant jaundice.

In the present study, the cord bilirubin level of > 2.5 mg/dL had the higher specificity (95.7%), negative predictive value (91.8) and fairly better positive predictive

value (68.2%) in predicting significant hyperbilirubinaemia of ≥ 17 mg/dL at 72 hours of life, which is comparable to other similar studies.^{12,13,14} Term healthy newborns having cord bilirubin value < 2 mg/dL had only 2.8% risk of developing significant hyperbilirubinaemia when compared to newborns with cord bilirubin > 2.5 mg/dL who had 68.2% risk of developing hyperbilirubinaemia, which was statistically significant ($p < 0.005$).

Thus, babies with cord bilirubin level > 2.5 mg/dL should be followed more frequently to reduce bilirubin-induced brain damage. In our study, there were no significant difference between the cases who did and who did not develop significant hyperbilirubinaemia with respect to factors such as gestational age, gender, birth weight, cord haematocrit level and maternal factors. Our study involved only healthy term newborns. Therefore, data cannot be applied to sick neonates and preterm babies. However, these babies are unlikely to discharge early from the hospital.

CONCLUSION

Babies with Umbilical Cord Bilirubin (UCB) level of < 2 mg/dL can be safely discharged early from hospital and babies with UCB > 2.5 mg/dL should be monitored for jaundice in hospital. Newborns with UCB between 2 to 2.5 mg/dL if discharged early can be asked for early review.

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