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Research Article

Cord Blood Albumin Level as a Predictor of Neonatal Jaundice-A Prospective Observational Study

Teena Nagar[1*], Rakesh Sharma[2], Kapoor Chand Meena[2], Rajendra Prasad Nagar[2]

[1]Department of Obstetrics and Gynecology, Jhalawar Medical College, Jhalawar, Rajasthan, India; [2]Department of Pediatrics, Jhalawar Medical College, Jhalawar, Rajasthan, India

ABSTRACT

Introduction: Neonatal jaundice is one of the most common conditions requiring medical attention in newborn babies. Early prediction and identification of severe neonatal jaundice for that age and appropriate treatment are must to prevent kernicterus, avoidance of aggressive management, maternal anxiety, and unnecessary expenditure and to reduce the duration of hospital stay.

Aims and objectives: To study the association between various levels of cord blood albumin and significant neonatal hyperbilirubinemia requiring interventions.

Material and methods: It was a prospective observational study and 404 single live born healthy neonates delivered normal or by cesarean section in hospital were included over a period of one year. Statistical analysis was done by SPSS (Statistical Package for the Social Science) software (20.0 trial version).

Results: Out of the total 404 neonates enrolled, 35 (8.7%) developed Neonatal Hyperbilirubinemia (NNH) and all received phototherapy. No one had exchange transfusion. Males to female ratio were 1:1.3. Cord serum albumin level of less than 2.8 gm/dL has a correlation with incidence of significant hyperbilirubinemia in term new-borns (P value is <0.0001). The sensitivity and specificity of cord albumin in detecting neonatal hyperbilirubinemia was determined to be 91.43% and 82.38% respectively. The positive and negative predictive value of cord albumin in detecting neonatal hyperbilirubinemia was determined to be 99.02% and 83.17% respectively.

Conclusion: Serum albumin level can be used as risk indicator to predict the development of significant hyperbilirubinemia. Thereby reducing the chance of kernicterus, being less invasive, easy to perform, and cost effective, cord serum albumin screening in NNH is very economical.

Keywords: Cord blood albumin; Risk factor; Neonatal jaundice; Serum bilirubin

INTRODUCTION

Neonatal jaundice is one of the most common conditions requiring medical attention in newborn babies. About 60% of neonates born at term and 80% of neonates born before term (preterm) develop jaundice [1]. Early prediction and identification of severe neonatal jaundice for that age and appropriate treatment are must to prevent kernicterus, avoidance of aggressive management, maternal anxiety, unnecessary expenditure and to reduce the duration of hospital stay [2,3]. Over 6.1% of well term new-borns have a serum bilirubin over 12.9 mg/dL, serum bilirubin over 15 mg/dL is found in 3% to 5% of normal term new-borns [4].

It is a common practice now days that healthy term new-borns by normal vaginal delivery are discharged early because of medical and social reasons [5]. According to American Academy of Pediatrics recommendation, every newborn discharged within 48 hrs should have follow up visit after 48 hrs to 72 hrs to look for any significant jaundice and other problems [6].

Albumin is the major protein present in abundant amount in the blood and has the property of binding to many hormones and nutrients [7]. Albumin has a specific site for binding with

Correspondance to: Teena Nagar, Department of Obstetrics and Gynecology, Jhalawar Medical College, Jhalawar, Rajasthan, India; E-mail: nagardrrajendra@gmail.com

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bilirubin and is responsible for transporting it to the liver and its clearance, its flexible structure helps it to adapt readily to ligands and it has three domains in its structure which offers a different kind of binding site. Bilirubin that is bound to be an albumin does not enter in brain [8].

There is paucity of studies on cord blood albumin as a predictor of severity of neonatal jaundice. Hence the present study is conducted to determine whether cord blood albumin helps in predicting subsequent development of neonatal jaundice that requires interventions like phototherapy or exchange transfusion.

MATERIALS AND METHODS

It was a prospective observational study carried out in Special Newborn Care Unit, Department of Pediatrics, Janana hospital Jhalawar Medical College and associated Hospital, Jhalawar over a period of one year. A total number of 404 new-borns were included in the study.

Inclusion criteria

1. Term babies of both genders.

2. Mode of delivery (normal or cesarean section).

3.Birth weight >2499gms.

4. APGAR 7/10 or more at 1 min.

Exclusion criteria

1. Non availability of consent.

2. ABO and Rh incompatibility.

3. Preterm.

4. Instrumental delivery (forceps and vacuum).

5. Neonatal sepsis.

6. Birth asphyxia.

7. Respiratory distress.

8. Major congenital anomalies.

9. Jaundice on first day of life.

Sampling was done by Simple random method and sample size calculated statistically was 404 (keeping the confidence interval 95% and prevalence or proportion 50%). Approval of ethical committee was obtained.

Methods

After obtaining inform consent from mother/parents' cases were subjected to full history emphasis on the antenatal and perinatal history (maternal illness, maternal drugs and fever), risk factors for hyperbilirubinemia e.g., ABO or RH incompatibility. Detail data of mother were also recorded in proforma. Thorough clinical examination was done for all included Cord blood samples (2 ml) were collected from all new-borns that complied with the protocol inclusion criteria. The samples were sent for the assaying of total, unconjugated, conjugated bilirubin and albumin levels. Bilirubin analyzed by Colorimetric Diazo method using semiautomated analysis, diazotized sulphanilic acid reaction using diamond reagent. Albumin analyzed by semi-automated bromcresol green dye-binding technique using diamond reagent.

Babies blood groups done manually and also rhesus D blood group analysis were made manually. All enrolled baby were followed up for 3 days and clinical assessment for jaundice was done according to Kramer dermal scale and by transcutaneous bilimeter. Under aseptic precaution 1ml venous blood was drawn from all the babies enrolled in study on 72 hours of life for serum bilirubin level. Sample was sent earlier (on 2nd or 3rd day) if transcutaneous bilimeter shows significant NNH. We have considered peak Serum bilirubin level>12 mg/dl on the day 2, >15 mg/dl on day 3, and 17 mg/dl on day 4 as a "Significant Hyperbilirubinemia" since specific treatment is usually considered at or above this level [9,10].

Statistical analysis was done by SPSS (Statistical Package for the Social Science) software (20.0 trial version). Unpaired T test and Chi Square test is used in data analysis. P value <0.05 is considered as significant.

RESULTS

A total of 404 normal healthy term new-borns were evaluated in Jhalawar Medical College, Jhalawar for Neonatal Hyperbilirubinemia (NNH) using cord serum albumin and Total Serum Bilirubin (TSB) level. Maximum cord blood albumin recorded was 4.4 gm/dl and minimum were 2.1 gm/dl. Birth weight of newborn was between 2500 gm to 3600 gm (Table1).

Table 1: Distribution of study parameters.

Parameters	Minimum	Maximum	Mean	Std. Deviation
Mother age (years)	20	34	24.7351	2.82081
Weight of mother (Kg)	54.5	84.5	69.0428	6.21395
Birth weight (Kg)	2.5	3.6	2.8231	0.28005
Gestational age (weeks)	37	41	38.6312	1.29328
Cord blood albumin (gm/dL)	2.1	4.4	3.0923	0.50197

Males to female's ratio were 1:1.308. Out of the total 404 neonates enrolled, 35 (8.7%) developed NNH. All the babies who had NNH received phototherapy. In male baby 18 (7.9%) developed NNH and in female baby 17 (9.7%) developed NNH and the difference was not statistically significant (P value=0.512) (Table 2).

Table 2: Distribution of NNH according to newborn sex.

Baby sex	NNH		Total	Chi sq	P value
	No	Yes			
Female	158	17	175		
	90.30%	9.70%	100.00%		
Male	211	18	229	0.431	0.512
	92.10%	7.90%	100.00%		
Total	369	35	404		
	91.30%	8.70%	100.00%		

In our study neonates were divided in 3 categories based on birth weight. Category I is 2500-3000 gm, category II is 3100-3500 gm, and category III is >3500 gm. In category I 30 (9.7%), in category II 5(5.3%) developed NNH and in category III no neonate developed NNH. Birth weight and NNH is found to have no correlation (P=0.380) (Table 3).

Table 3: Distribution of NNH according to birth weight.

Birth weight	NNH		Total	Chi sq	P value
	No	Yes			
2.5-3.0 kg (Category I)	278	30	308		
	90.30%	9.70%	100.00%		
3.1-3.5 kg (Category II)	90	5	95	1.934	0.38
	94.70%	5.30%	100.00%		
>3.5 kg (Category III)	1	0	1		
	100.00%	0.00%	100.00%		
Total	369	35	404		
	91.30%	8.70%	100.00%		

in primary gravida 14 (8%), and in Gravida 2nd 17(10.1%), in Gravida 3rd 2(5%), in Gravida 4th 1(7.1%), in Gravida 5th 1(25%) and in Gravida 6th 0 (none) developed NNH. Gravida of mother and NNH is found to have no correlation (P value=0.747) (Table 4).

New born were divided in five groups (37 completed weeks to 41 completed weeks) based on gestational age. After statistical evaluation of these children, the gestational age and NNH is found to have no correlation (P value=0.509) (Table 5).

We grouped our sample into 3 groups according their cord blood albumin level group I being <2.8 gm/dL, group II 2.8-3.3

Table 4: Distribution of NNH according to gravida.

Gravida	NNH		Total	Chi sq	P value
	No	Yes			
1	162	14	176		
	92.00%	8.00%	100.00%		
2	152	17	169		
	89.90%	10.10%	100.00%	2.691	0.747
3	38	2	40		
	95.00%	5.00%	100.00%		
4	13	1	14		
	92.90%	7.10%	100.00%		
5	3	1	4		
	75.00%	25.00%	100.00%		
6	1	0	1		
	100.00%	0.00%	100.00%		
Total	369	35	404		
	91.30%	8.70%	100.00%		

Table 5: Distribution of NNH according to gestational age.

Gestational age (weeks)	NNH		Total	Chi sq	P value
	No	Yes			
37	87	11	98		
	88.80%	11.20%	100.00%		
38	93	8	101		
	92.10%	7.90%	100.00%		
39	92	9	101	3.297	0.509
	91.10%	8.90%	100.00%		
40	54	6	60		
	90.00%	10.00%	100.00%		
41	43	1	44		
	97.70%	2.30%	100.00%		
Total	369	35	404		
	91.30%	8.70%	100.00%		

gm/dL, and group III >3.3 gm/dL. Out of the total 404 neonates enrolled, 97 (24%) belonged to group I (albumin <2.8 gm/dL), 207(51.2%) to group II (2.8-3.3 gm/dL), and 100(24.8%) to group III (>3.3 gm/dL) (Table 6).

Table 6: Distribution of cord blood serum albumin of babies.

Cord blood serum albumin(gm/dL)	Frequency	Percent
< 2.8	97	24
2.8 - 3.3	207	51.2
>3.3	100	24.8
Total	404	100

Out of the total 97 neonates in group I, 32 (91.4%) developed NNH. Out of the total 207 neonates in group II, 3(8.6%) developed NNH and out of the total 100 neonates in group III, no one developed NNH. P value is <0.0001, which is significant and shows that cord serum albumin level of <2.8gm/dL has a correlation with incidence of significant hyperbilirubinemia in term new-borns (Table 7).

Table 7: Distribution of NNH according to cord blood serum albumin.

Cord blood serum albumin(gm/dL)	NNH		Total	Chi sq	P value
	No	Yes			
< 2.8	65	32	97		
	17.60%	91.40%	24.00%		
2.8 - 3.3	204	3	207		
	55.30%	8.60%	51.20%	95.642	<0.0001*
>3.3	100	0	100		
	27.10%	0.00%	24.80%		
Total	369	35	404		
	100.00 %	100.00 %	100.00 %		
Statistic			Value		
Sensitivity			91.43%		
Specificity			82.38%		
Positive Predictive Value (*)			32.99%		
Negative Predictive Value (*)			99.02%		
Accuracy (*)			83.17%		

The sensitivity and specificity of cord albumin in detecting neonatal hyperbilirubinemia in this study was determined to be 91.43% and 82.38% respectively. The positive and negative predictive value of cord albumin in detecting neonatal hyperbilirubinemia in this study was determined to be 99.02% and 83.17% respectively. Cord blood albumin also statistically correlation with duration of phototherapy in term new-borns (P value is <0.0001). Lower the cord serum albumin longer phototherapy required (Table 8).

Table 8: Distribution of duration of phototherapy given in days according to cord blood serum albumin.

Duration of phototherapy given in days	Cord blood serum albumin(gm/dL)			Total	Chi sq	P value
	< 2.8	2.8 - 3.3	>3.3			
1	27	3	0	30		
	90.00%	10.00%	0.00%	100.00 %		
2	5	0	0	5		
	100.00 %	0.00%	0.00%	100.00 %	95.904	<0.0001*
No	65	204	100	369		
	17.60%	55.30%	27.10%	100.00 %		
Total	97	207	100	404		
	24.00%	51.20%	24.80%	100.00 %		

DISCUSSION

A total of 404 normal healthy term new-borns were evaluated in Jhalawar Medical College, Jhalawar for neonatal hyperbilirubinemia using cord serum albumin and Total Serum Bilirubin (TSB) level.

Even though the primary aim was to find out correlation between cord serum albumin and NNH, we also analysed the relationship, sex of the babies, birth weight, gravida, gestation and NNH. Also, the percentage of phototherapy required and percentage of exchange transfusion totally carried out in the study are also analysed.

In our study, there were 229(56.7%) male child and 175(43.3%) female new-borns. After statistical evaluation of these children (P value=0.512), the sex and NNH is found to have no such correlation. Reshad M et al. [11] conducted A study on 150 neonates and there was no significant association between gender and NNH in either of the two groups (P value=0.955 in term and 0.343 in preterm). Likewise, Kumar et al. [12] also find association (P value=0.93) between gender as well as neonatal hyperbilirubinemia, among term new-borns.

Regarding the birth weight of the child, in our study neonates were divided in 3 categories based on weight and development of NNH. After statistical evaluation of these children, the birth weight and NNH is found to have no correlation (P value=0.380). Rajkumar M. Meshram et al. [13] conducted similar study on 1040 neonates. There was no statistical difference in development of NNH and birth weight (P value>0.05).

In our study number of gravid has no statistically correlation with NNH correlation (P value=0.747). Kumar et al. [12] did a study in neonates and in primi 9 (13.4%), in G2 3(15%) and in G3 2 (15.4%) developed NNH. there is no association (P value = 0.97) between birth order and neonatal hyperbilirubinemia among term new-borns. Likewise, Rafi M et al. [14] in their study on 300 term neonates, found no significant association (P value=0.485) between the neonatal hyperbilirubinemia and parity of mother.

In our study gestational age was 37-41 week (Term neonate). There was no significant statistical association between gestation age and NNH (P value=0.509). Likewise, Kumar et al. [12] studied 100 neonate of different gestational age and did not show any significant difference for development of hyperbilirubinemia and gestational age. (P value=0.33).

Out of the total 404 neonates enrolled, 97 (24%) belonged to group I (albumin<2.8 gm/dL), 207 (51.2%) to group II (2.8-3.3 g/dL), and 100 (24.8%) to group III (>3.3 g/dL). Out of the total 97 neonates in group I, 32 (91.4%) developed NNH out of which 5 (15.62%) at 24-48 hours, 12 (37.5%) developed NNH at 48-72 hours and 15 (46.87%) developed NNH at >72 hours. All the 32 neonates developed hyperbilirubinemia required phototherapy. There was no requirement of exchange transfusion in our study.

The sensitivity and specificity of cord albumin in detecting neonatal hyperbilirubinemia in this study was determined to be 91.43% and 82.38% respectively. The positive and negative predictive value of cord albumin in detecting neonatal hyperbilirubinemia in this study was determined to be 99.02% and 83.17% respectively. P value is <0.0001, which is significant and shows that cord serum albumin level of <2.8gm/dL has a correlation with incidence of significant hyperbilirubinemia in term new-borns.

Mohamed Reshad et al. [11] conducted similar study on 150 neonates divided in to term (75) and preterm (75). They were further divided into 3 groups based on Cord Blood Albumin level (CBA). They also reported that in term and preterm baby who has CBA<2.8 gm/dL developed neonatal hyperbilirubinemia. The P value was significant (0.001). None of the new-borns with CSA level >3.4 gm/dL developed neonatal hyperbilirubinemia.

Chaudhry et al. [15] conducted study to determine significance of cord blood albumin estimation as a predictor of neonatal jaundice and found that lower is the albumin level higher the chance of developing neonatal jaundice and requiring intervention (P value of <0.05).

Praveena et al. [16] in their study divided neonates in two groups based on cord blood albumin level and concluded that among those having cord albumin level of the <2.8gm/dL, 92.5% had a jaundice while those who had >2.8gm/dL, 8.9% only can be developed jaundice. Sensitivity was found to be 69.44%, Specificity was 98.24%, positive predictive value was 92.59% and negative predictive value was 91.05%. Area under the curve was found to be 0.876. There was a significant P value of <0.05.

CONCLUSION

NNH is a very common problem. It is also the most common cause of readmission in the first week of life. Neonates with NNH had significantly lower levels of cord serum albumin (<2.8 gm/dL). So, it is possible to define a group of neonates at risk of developing jaundice needing phototherapy at birth. Knowledge of risk factors of NNH in neonates could influence decision of early discharge vs. prolonged observation. Being easy to perform these values may be extrapolated in the outreach rural population for better screening of NNH.

Limitations of our study were that only healthy term babies were taken into consideration and other confounding factor were also not included properly. So much bigger cohort of different gestational age and inclusion of other associated factor are needed to generalized the results.

REFERENCES

1. Rennie J, Burman Roy S, Murphy MS. Guideline Development Group. Neonatal jaundice: summary of NICE guidance. BMJ. 2010; 340:1190-1196.
2. Newman TB, Escobar GJ, Gonzales VM, Armstrong MA, Gardner MN, Folck BF. Frequency of neonatal bilirubin testing and hyperbilirubinemia in a large health maintenance organization. Pediatrics. 1999;104:1198-203.
3. Bhutani VK, Johnson L, Sivieri EM. Predictive ability of a predischarge hour-specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near-term new-borns. Pediatrics. 1999 ;103:6-14.
4. Ahlfors CE. Criteria for exchange transfusion in jaundiced new-borns. Pediatrics. 1994;93(3):488-494.
5. Ip S, Chung M, Kulig J, O'Brien R, Sege R, Glicken S, et al. An evidence-based review of important issues concerning neonatal hyperbilirubinemia. Pediatrics. 2004;114(1):e130-53.
6. Venkatamurthy M, Murali SM, Mamatha S. A comparison study: cord serum albumin is compared with cord serum bilirubin as a risk indicator in predicting neonatal jaundice. J Evolut Med Dent Sci. 2014;3(15):4017-4023.
7. Roche M, Rondeau P, Singh NR, Tarnus E, Bourdon E. The antioxidant properties of serum albumin. FEBS letters. 2008 ; 582:1783-1787.

8. Nikolaev AV, Rozhilo YA, Starozhilova TK, Sarnatskaya VV, Yushko LA, Mikhailovskii SV, et al. Mathematical Model of Binding of Albumin–Bilirubin Complex to the Surface of Carbon Pyropolymer. Bull Exp Biol Med. 2005;140(3):365-369.
9. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term new-borns. Pediatrics. 1995;96:730-733.
10. van de Steeg E, Stránecký V, Hartmannová H, Nosková L, Hřebíček M, Wagenaar E, et al. Complete OATP1B1 and OATP1B3 deficiency causes human Rotor syndrome by interrupting conjugated bilirubin reuptake into the liver. J Clinic Investigat. 2012;122:519-528.
11. Reshad M, Ravichander B, Raghuraman TS. A study of cord blood albumin as a predictor of significant neonatal hyperbilirubinemia in term and preterm neonates. Int J Res Med Sci. 2016 Mar;4:887-890.
12. Kumar S, Agrawal K, Chaturvedi A. Prediction of significant neonatal hyperbilirubinemia on the basis of cord serum albumin level in healthy term neonates. IOSR J Dent Med Sci. 2018; 4:57-62.
13. Rajkumar MM, Saira Merchant, Sartajbegam N P. Utility of Cord Blood Albumin as a Predictors of Significant Neonatal Hyperbilirubinemia in Healthy Term Neonate. Asian J Clinical Pediatrics Neonatol. 2019; 7:17-21
14. Erum Rashid Chaudhry, Abdul Khaliq Naveed, Amena Rahim. Decreased Cord Blood Albumin: A Predictor of Neonatal Jaundice. JIIMC. 2016; 11:149-52.
15. Praveena, R Ramanathan. Cord Blood Albumin as Predictor of Neonatal Hyperbilirubinemia. JMSCR.2017; 5:904-909.