Research Article

OBSERVATIONAL STUDY OF ESTIMATION AND EVALUATION OF CORD SERUM ALBUMIN LEVEL AS A RISK INDICATOR OF NEONATAL HYPERBILIRUBINEMIA

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ABSTRACT

Introduction: Neonatal Hyperbilirubinemia is a common physical finding during the first week of life. Among 4% of term newborns who are readmitted to the hospital during their first week of life approximately 85% are for Jaundice as the cause. The option of predicting the future development of neonatal hyperbilirubinemia is the best alternative to diagnose babies at risk and prevent the comorbidities.

Aims and Objectives: To study the relationship between various levels of cord serum albumin and development of significant neonatal hyperbilirubinemia.

Materials and Methods: Cord serum albumin level was estimated at birth in term babies without any co-morbity after obtaining informed consent from parent.Total serum bilirubin estimation was done at 72-96 hours of age. All the babies were followed up daily for first 4 postnatal days and assessed for development of neonatal hyperbilirubinemia.

Results: Among children with serum albumin level <2.8 g/dl (screen positive), 22.2% had significant hyperbilirubinemia. Among children with serum albumin > 2.8 g/dl (screen negative), this proportion was only 5.6%. The association between the albumin and total bilirubin was statistically significant with chi-square value 12.397 and P-value <0.001.

Conclusion: Early detection of babies who develop significant neonatal hyperbilirubinemia helps in starting treatment early and thus preventing the consequences like kernicterus. Umbilical cord serum albumin level ≥3.4g/dl can be considered safe and such term babies can be discharged early.

INTRODUCTION

Neonatal Hyperbilirubinemia is a common physical finding during the first week of life.[1] Many times it is physiological in the newborn because liver is not mature enough to handle the bilirubin. During the first week of life, neonatal hyperbilirubinemia affects nearly 60% of term and 80% of pre-term neonates. 6.1% of term newborn have a serum bilirubin over 12.9mg% and 3% of newborns have serum bilirubin over 15mg%. Neonatal hyperbilirubinemia is the most common cause in 6.5% of babies for readmission during the early neonatal period.[2] Among 4% of term newborns who are readmitted to the hospital during their first week of life, approximately 85% are for jaundice as the cause.[3] The main concern for parents as well as pediatricians is the development of neonatal hyperbilirubinemia[4] and its consequences. American Academy of Pediatrics recommends that newborns discharged within 48 hours of life should have a follow-up visit after 48 to 72 hours to look for any significant jaundice and other problems.[5] During neonatal period, metabolism of bilirubin is in transition from the fetal stage to adult stage.

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Metabolism of bilirubin takes place in liver which is not mature enough to handle the bilirubin. There is an increased load of bilirubin due to a higher circulating erythrocyte volume, a shorter erythrocyte life span and a large amount of early-labeled bilirubin. Albumin is a major binding protein in the neonate. Low production of albumin will lower its transport and binding capacity, especially in preterm neonates.[6,7]

Discharging babies in the early stages from the hospital has created more difficulties in neonatal hyperbilirubinemia recognition, follow-up, early treatment and prevention of bilirubin induced encephalopathy. The option of predicting the future development of neonatal hyperbilirubinemia is the best alternative to diagnose babies at risk and prevent the comorbidities.

MATERIALS AND METHODS

The study was conducted over a period of 1 year from March 2015 to March 2016 in the department of paediatrics in SreeBalaji medical college and hospital. Cord serum albumin level was estimated in 198 term babies with birth weight > 2.5 kg and normal Apgar score. The babies were followed and total serum bilirubin estimation was done at 72-96 hours of

age.Cord blood albumin levels were considered as the primary explanatory parameter. Serum bilirubin levels were considered as the primary outcome parameter.All the variables were summarized by using mean and standard deviation for quantitative variable, frequency and proportion for categorical variables. The serum bilirubin values above 17 mg/dl were considered as significant hyperbilirubinemia. Receiver Operating Curve (ROC) analysis was carried out to estimate the overall predictive value. The predictive validity of different levels of cord blood albumin levels was assessed by calculating sensitivity, specificity, and predictive values along with their 95% CI (Confidence Interval). IBM SPSS version 21 was used for statistical analysis.

RESULTS

A total of 198 newborns were included in the analysis. The proportion of male participants were 54.55% and females were 45.45% in the study population. The number of participants with normal delivery and LSCS were 129 (65.15%) and 69 (34.85%) respectively in study population. The mean birth weight of the babies was 2.920 ± 0.354 in study population. The mean albumin level was 2.978 ± 0.576. The mean total and direct bilirubin levels were 13.25 ± 2.071 and 13.25 ± 0.232 respectively in study population (Table 1).

Table 1 Descriptive analysis of blood parameters in study group (N=198)

Parameter	Mean±STD	Median	Max	Min	95% C.I.for EXP(B) Lower	Upper
Baby's Birth Weight	2.920 ± 0.354	2.80	4.00	2.50	2.87	2.97
Albumin	2.978 ± 0.576	2.92	5.21	1.69	2.90	3.06
Total Bilirubin	13.25 ± 2.071	13.01	18.91	5.70	12.96	13.54
Direct Bilirubin	13.25 ± 0.232	1.27	2.40	0.71	1.25	1.31

The proportion of participants with cord serum albumin below 2.8 level was 36.4%. The proportion of participants at the range of 2.9 to 3.39 was 35.9% and the proportion of participants above 3.4 level was 27.8% in study population (Table 2).

Table 2 Frequency distribution of Cord Albumin in study group (N=198)

Albumin	Frequency	Percentage
<2.8	72	36.4
2.9 to 3.39	71	35.9
>3.4	55	27.8

The number of children, who had significant hyperbilirubinemia was 23 (11.62%) in study population (Table 3).

Table 3 Descriptive analysis of total bilirubin in study group (N=198)

Total Bilirubin	Frequency	Percentage
Significant Hyperbilirubinemia	23	11.62%
No Hyperbilirubinemia	175	88.38%

Among children with serum albumin level <2.8gm/dl (screening positive), 22.2% of them had significant hyperbilirubinemia. Among screening negative children this proportion was only 5.6%. The association between the albumin and total bilirubin were statistically significant (The chi-square value 12.397 P-value <0.001) (Table 4). Cord blood albumin as a screening test had a sensitivity of 69.57%,

specificity was 68.00%, False positive rate was 32.0% and False negative rate was 30.43%.

Table 4 Association between serum albumin and total bilirubin in study group (N=198)

Albumin (2.8)	Total bilirubin (17)		Chi square	P value
	Significant Hyperbilirubinemia	No Hyperbilirubinemia		
Screening Positive (<2.8)	16 (22.2%)	56 (77.8%)		
			12.397	<0.001
Screening Negative (2.8 and above)	7 (5.6%)	119 (94.4%)		

The Positive predictive value & Negative predictive value was 22.22% and 94.44% respectively. The Diagnostic accuracy was 68% (Table 5).

Table 5 Validity of cord blood albumin (< 2.8) as a screening test in study group (N=198)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	69.57%	50.76%	88.36%
Specificity	68.00%	61.08%	74.91%
False positive rate	32.00%	25.08%	38.91%
False negative rate	30.43%	11.63%	49.23%
Positive predictive value	22.22%	12.61%	31.82%
Negative predictive value	94.44%	90.44%	98.44%
Diagnostic accuracy	68%	61.69%	74.66%

The proportion of children, who developed significant hyperbilirubinemia was 22.2% in people with albumin < 2.8. This proportion was 5.65 in people with cord blood albumin between 2.8 to 3.39 and 5.5% in people with cord blood albumin 3.4 and above. This association was statistically significant. (P value = 0.002) (Table 6).

Table 6 Association between Cord Albumin and total bilirubin in study group (N=198)

Cord Albumin	Total Bilirubin		Chi-Square	P value
	Significant Hyperbilirubinemia	No Hyperbilirubinemia		
< 2.8	16 (22.2%)	56 (77.8%)		
2.9 to 3.39	4 5.6%	67 94.4%	12.397	0.002
> 3.4	3 5.5%	52 94.5%		

DISCUSSION

The word 'Jaundice' derived from the French word 'Jaune' meaning yellow.[8] Halbrecht coined the term "Icterus Precox" for jaundice that developed within 24 hours of birth.[9] Neonatal hyperbilirubinemia is one of the most common causes for readmission of the newborns. The need for early detection of hyperbilirubinemia in the newborns discharged early from the hospital is therefore important.

In the present study conducted on 198 newborns, 27 of them developed significant neonatal hyperbilirubinemia requiring phototherapy. The study population is divided into 3groups on the basis of cord blood albumin. Group 1-Cord serum albumin-≤2.8gm/dl, Group 2- Cord serum albumin- 2.9-3.3gm/dl, Group 3- Cord serum albumin - ≥3.4gm/dl. 19 newborns (70.3%) had cord serum albumin levels <2.8g/dl, 5 newborns (18.5%) had cord serum albumin levels between 2.9 to 3.3g/dl, and 3 newborns (11.11%) had cord serum albumin

levels >3.4gm/dl. In our study in neonates of cord serum albumin of <2.8gm/dl have sensitivity of 69.57%, specificity of 68.00%, positive predictive value is 22.22% and negative predictive value is 94.44%. The present study results are correlated well with Sahu *et al*[10] conducted in 2011, Trivedi *et al*[11] in 2013, Venkatamurthy *et al*[12] in 2013, Gothami *et al*[13] in 2015 and Shagungupta *et al*[14] in 2016. Thus cord serum albumin level appears a risk indicator in predicting neonatal hyperbilirubinemia. Hence this study indicates that cord serum albumin level ≤ 2.8g/dl is high risk factor for future development of neonatal hyperbilirubinemia and cord serum albumin level ≥ 3.4g/dl is probably safe for early discharge.

CONCLUSION

Neonatal hyperbilirubinemia occurs in 60% of term neonates. Among 4% of term neonates who are readmitted to the hospital during the first week of life, approximately 85% of them are for jaundice. Early detection of babies who develop significant neonatal hyperbilirubinemia helps in starting treatment early and thus preventing the consequences like kernicterus. Umbilical cord serum albumin level of ≤ 2.8g/dl has a correlation with incidence of significant hyperbilirubinemia in term newborns. So the cord serum albumin level of ≤ 2.8g/dl can be used as a risk indicator to predict the development of significant hyperbilirubinemia, and such babies can be observed in the hospital upto 4 days of life (peak time for neonatal hyperbilirubinemia) to prevent later readmission for neonatal hyperbilirubinemia and the dangerous consequences of it like kernicterus.

References

1. Meharban Singh. Care of the Newborn. 7[th]ed. New Delhi: Sagar Publications; 2010. Chapter 18, Neonatal Jaundice, p 254-74.
2. Radmacher P, Massey C, Adamkin D. Hidden Morbidity With ''Successful'' Early Discharge. *J Perinatol.* 2002; 22:15-20.
3. Kiely M, Drum MA, Kessel W. Early discharge, risks, benefits and who decides. *Clinperinatol.* 1998 Sep; 25(3):539–53.
4. Cloharty JP, Stork AR, Eichenwald EC, Hansen AR. Manual of neonatal care. 7th edn, Philadelphia: Lippincott Willams and Wilkins; 2012. Chapter 26, *Neonatal Hyperbilirubinemia*; p. 304 -339.
5. American Academy Of Pediatrics, Clinical Practice Guideline; Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation, *Pediatrics* 2004; 114(1):297-316.
6. Penn AA, *et al*. Kernicterus in a full term infant. *Pediatrics* 1994; 93:1003-1006.
7. Maisels MJ, *et al*. Kernicterus in otherwise healthy breast-fed term newborns, *Pediatrics* 1995; 96: 730-733.
8. AshimaMadan, James R.Macmohan, and David K. Stevenson. Neonatal Hyperbilirubinemia in the Newborn. In: Taeusch, Ballard, Gleason. Avery's Diseases of the Newborn 8th edn, 1226-1257.
9. Halbrecht L. Role of hemagglutinins anti-A and anti-B in pathogenesis of jaundice of newborn (icterus neonatorumprecox). *Amer J Dis Child* 1944; 68: 248.
10. SuchandaSahu *et al*, Cord blood albumin as a predictor of neonatal jaundice, International *J.Biological and medical research* 2011; 2(1):436-438.
11. Treivedi *et al*, Cord Serum bilirubin and Albumin in Neonatal Hyperbilirubinemia, *International Journal of Integrative sciences, Innovation and technology*. 2013; 2(2):39-42.
12. Venkatamurthy M *et al*, Evaluation of cord serum albumin level as a risk indicator in predicting neonatal jaundice: *International Journal of Health Information and Medical Research* Vol: 1, Issue: 1, Jan 2014.
13. GothamiSandhyaDwarampudi and N. Ramakrishna. cord blood albumina and bilirubin levels as predictors in neonatal hyperbilirubinemia: *Int J Pharm Bio Sci* 2015 July ; 6(3): (B) 273 - 279.
14. Shagungupta *et al*, Neonatal hyperbilirubinemia after induction of labour with oxytocin and cord serum albumin is compared with cord serum bilirubin as a risk indicator: *International Journal of Biomedical Research* 2016; 7(7): 435-438.

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