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Original Research Article

Association of cord serum albumin with neonatal hyperbilirubinemia among term-neonates

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ABSTRACT

Background: NH affects nearly 60% of term and 80% of preterm neonates during first week of life. 6.1% of well term newborn have a serum bilirubin over 12.9 mg%. Serum bilirubin over 15 mg% is found in 3% of normal term newborns. Neonatal Hyperbilirubinemia (NH) is a cause of concern for the parents as well as for the paediatricians. Aim of study to find out the association between various levels of cord serum albumin (CSA) and significant neonatal hyperbilirubinemia requiring interventions like phototherapy or exchange transfusion and whether it can be used as a risk indicator for subsequent development of significant jaundice.
Methods: The present study was conducted on 150 randomly selected eligible term neonates delivered at Department of Pediatrics, Rajkiya Mahila Chikitsalaya, JLN Medical College and Associated Group of Hospitals, Ajmer, India.
Results: Authors conducted a prospective study on 150sequentially born term babies. Cord blood was collected at birth and cord serum albumin estimation was done within 4-6 hours of collection of the blood. Cohort was grouped into Group 1, Group 2 and Group 3 based on CSA level ≤ 2.8g/dl, 2.9-3.3g/dl and ≥ 3.4 g/dl respectively. Knowledge of risk factors of NH in neonates could influence decision of early discharge vs. prolonged observation cord serum albumin level of ≤ 2.8g/dl has a correlation with incidence of significant hyperbilirubinemia in term newborns. So this ≤ 2.8g/dl of cord serum albumin level can be used as risk indicator to predict the development of significant hyperbilirubinemia. Whereas cord serum albumin level ≥3.4g/dl is considered safe.
Conclusions: Term neonates with hyperbilirubinemia with a total serum bilirubin level ≥17 mg/dl had levels of cord serum albumin of ≤ 2.8 g/dl, and this can be used as a risk indicator to predict the development of NH.

Keywords: Cord serum albumin, Neonatal hyperbilirubinemia, Total serum bilirubin

INTRODUCTION

Neonatal Hyperbilirubinemia (NH) is commonest abnormal physical finding during the first week of life. Over two third of newborn babies develop clinical jaundice. The physical finding like yellowish discoloration of the skin and sclera in newborns is due to accumulation of unconjugated bilirubin. In most infants, unconjugated hyperbilirubinemia reflects a normal physiological phenomenon.[1]

NH affects nearly 60% of term and 80% of preterm neonates during first week of life. 6.1% of well term newborn have a serum bilirubin over 12.9 mg%. Serum bilirubin over 15 mg% is found in 3% of normal term newborns. Neonatal Hyperbilirubinemia (NH) is a cause of concern for the parents as well as for the pediatricians.[2]

Early discharge of healthy term newborns after normal vaginal delivery has become a common practice, because of medical reasons like prevention of nosocomial infections, social reasons like in early naming ceremony, and also due to economical constrains.

In significant number (6.5%) of babies, Neonatal Hyperbilirubinemia (NH) is the most common cause for readmission during the early neonatal period.[3] Up to 4% of term newborns who are readmitted to the hospital during their first week of life, approximately 85% are for jaundice.[4]

American Academy of pediatrics recommends that newborn discharged within 48 hours should have a follow-up visit after 48 to 72 hours for any significant jaundice and other problems.[5]

This recommendation is not appropriate for our country due to limited follow- up facilities in the community. These babies may develop jaundice which may be over looked or delay in recognition, unless the baby is closely monitored.

Concern of pediatrician regarding the early discharge are reports of bilirubin induced brain damage occurred in healthy term infants even without hemolysis. The sequalae could be serious as it may results in cerebral palsy, sensorineural deafness and mental retardation.[6,7]

NH recognition, follow-up, early treatment and prevention of bilirubin induced encephalopathy has become more difficult as a result of earlier discharge from the hospital. The treatment of severe NH by exchange transfusion is costly. It is associated with complications, time consuming and requires skilled manpower. Early treatment of jaundice with phototherapy is effective, simple and cheap.

Developing countries like India must be fully aware of this limitation on the development of neonatal care, particularly neonatal intensive care. The ultimate aim should be to benefit maximum number of newborn babies with cost effective treatment protocol. He concept of prediction offers an attractive option to pick up babies at risk of neonatal hyperbilirubinemia.

Physical examination is not a reliable measure of the serum bilirubin. By predicting the newborns at risk for significant NH early at birth, we can design and implement the follow-up programme in these risk groups, cost effectively.

Aim of this study to find out the association between various levels of cord serum albumin (CSA) and significant neonatal hyperbilirubinemia requiring interventions like phototherapy or exchange transfusion and whether it can be used as a risk indicator for subsequent development of significant jaundice.

METHODS

The present study was conducted on 150 randomly selected eligible term neonates delivered at Department of Pediatrics, Rajkiya Mahila Chikitsalaya, JLN Medical College and Associated Group of Hospitals, Ajmer, Rajasthan, from Jan 2015 to December 2015.

Inclusion and exclusion criteria

Term babies of both genders delivered both normally or by caesarean section, with birth weight _2.5 kg and an Apgar score of _7/10 at 1 min, were included. All other babies, who were at more risk of developing jaundice because of their clinical status, were excluded. Babies with prematurity, Rh-negative mother, septicaemia, delivered by instrumentation, perinatal hypoxia, breathing difficulty, me conium aspiration syndrome, first day jaundice, cephalohematoma, diabetic mother, and twin to twin transfusion were excluded.

Data collection

An informed consent was obtained from the parents of the newborn before enrolling them in the study. Demographic profile and relevant information was collected by using structured Performa by interviewing the mother and from mother's case sheet Gestational age was assessed by New Ballard score (if LMP not sure). Cord Serum Albumin level was estimated at birth. Total Serum Bilirubin (TSB) estimation was done at 72-96 hours of age.

All the babies were followed up daily for first 4 postnatal days and babies mere daily assessed for NH and its severity. The serum albumin level was estimated from 2ml of cord blood sample collected from the placental end, after its separation. Venous blood samples were collected from the baby at 72-96 hr of life and analyzed for total and direct serum bilirubin and blood group.

Laboratory procedures

- Cord blood collected at birth was analyzed by auto analyzer method (RANDOX RXimola and RXmonza) for Cord Serum Albumin estimation.
- Venous blood sample collected was stored away from light. The sample was refrigerated between 2 -8 degree C till serum bilirubin estimation is done. Serum bilirubin estimation was done within 12 hours of collection of sample by Auto Analyser method.

Principle: Bilirubin reacts with diazotized sulfanilic acid to produce azobilirubin which is quantified by spectrometry. Both direct and indirect bilirubin couple with diazo in the presence of cetremide. The terms 'direct' and 'indirect' are approximately equivalent to conjugated and unconjugated fractions.

- Blood group of newborn analyzed by antisera method.

Principle: The red cells contain different types of agglutinogens (antigens) and plasma contains agglutinins (antibodies). The red cells of the subject are allowed to react with commercially made agglutinins (anti sera). The presence or absence of clumping of red cells in different agglutinins determines the blood groups.

Inference

The main outcome of the study was inferred in terms of neonatal hyperbilirubinemia.

Serum bilirubin ≥17 mg/dl after 72 hours of life was taken as hyperbilirubinemia and treatment is advised, as per the American academy of pediatrics practice parameter, 2004.

IAP-NNF also recommends considering Phototherapy with neonatal serum bilirubin levels of ≥17mg/dl after 72 hours of life.

So in the present study newborn with Total serum bilirubin level of ≥17mg/dl are considered hyperbilirubinemia and needs intervention (like Phototherapy or Exchange Transfusion) after 72 hours of postnatal life.

Statistical analysis

The main outcome of the study was inferred in terms of significant NH. All data collected were entered in excel sheet to prepare master chart. Continuous variables were summarized as mean and standard deviation, while nominal/categorical variables as percentage. Categorical variables related to baseline characteristics of enrolled neonates were analyzed for their distribution among different groups according to CSA level. Chi square test was used to assess the difference at significance level (p value <0.05)

RESULTS

The gender distribution of newborn in the study group; 85 (56.7%) were male and 65 (43.3%) were female newborns.

Majority of the newborn in the study group were delivered by vaginal route which constitutes 106 out of 150, i.e 70.7%. And <2.5kg birth weight babies were excluded. And among the study group 68.6% (n=103) newborns had birth weight between 2.5-3.0 kg. Group 1 consists of 67 newborns constituting to 44.6% of the study cohort.

Whereas Group 2 consists of 49 newborns (32.6%) and Group 3 consists of 34 newborns (22.8%) of study cohort.

Most of the newborn belong to O positive, which results to 61.4% of study cohort. Second most common blood group in this study cohort was B positive (20%). Total Serum Bilirubin level estimated at 72-96 hours of postnatal life in the study cohort. 18 out of 150 newborn developed NH (Table 1).

Table 1: Demographic and clinical presentation of study participates.

Variable	Numbers	Percentage (%)
Gender		
Male	85	56.7%
Female	65	43.3%
Total	150	100%
Mode of delivery		
Caesarean section	44	29.3%
Vaginal route	106	70.7%
Total	100	100%
Birth weight (kg)		
2.5-3	103	68.6%
3-3.5	41	27.4%
>3.5	6	4%
Total	150	100%
Cord serum albumin (g/dl)		
≤2.8 (Group 1)	67	44.6%
2.9-3.3(Group 2)	49	32.6%
≥3.4 (Group 3)	34	22.8
Total	150	100%
Baby blood group		
A+	31	20.7%
B+	30	20%
AB+	7	4.6%
O+	82	54.6%
Total	150	100%
Total serum Bilirubin (mg/dl)		
≤10	6	4%
10-14	114	76%
15-17	12	8%
≥17	18	12%
Total	150	100%

Table 2: Comparison of need for phototherapy with cord serum albumin level.

Phototherapy	Cord albumin levels			Total
	≤2.8	2.9-3.3	≥3.4	
No	50 (74.7%)	48 (97.9%)	34 (100%)	132 (88%)
Yes	17 (25.3%)	1 (2.1%)	0	18 (12%)
Total	67 (100%)	49 (100%)	34 (100%)	150 (100%)

The comparison between the newborns who developed significant NH requiring phototherapy and cord albumin

groups. Statistical significant is seen with p value <0.001 (Table 2).

Table 3: Correlation of clinical variable with need for phototherapy.

Variables	p		p value
	No (n=132)	Yes (n=18)	
Gender			
Male	75 (56.8%)	10 (55.5%)	0.889
Female	57 (43.2%)	8 (44.5%)	
Mode of delivery			
Ceserian section	39 (29.6%)	5 (27.8%)	0.943
Vaginal route	93 (70.4%)	13 (72.2%)	
Oxytocin drug use			
No	52 (39.4%)	8 (44.4%)	0.603
Yes	80 (60.6%)	10 (55.6%)	
Cord blood albumin(mg/dl)			
≤2.8	50 (37.9%)	17 (94.4%)	<0.001
2.9-3.3	48 (36.3%)	1 (5.6%)	
≥3.4	34 (25.8%)	0	
ABO incompatibility			
No	129 (97.7%)	17 (94.4%)	0.389
Yes	3 (2.3%)	1 (5.6%)	

The correlation of variables like gender, mode of delivery, oxytocin, cord albumin level and ABO incompatability with newborns who developed significant NH requiring phototherapy. Statistical significance is seen in cord albumin levels only (p<0.001) and there was no statistical significance with other variables (Table 3).

DISCUSSION

There is concern regarding early discharge of healthy term newborns due to reports of bilirubin induced brain damage resulting in sequalae like kernicterus. Kernicteus is the chronic sequelae of acute bilirubin encephalopathy. Incidence of kernicterus is unknown.

Hence defining a certain bilirubin level as physiological can be misleading and potentially dangerous. Neonatal hyperbilirubinemia is a potentially correctable and kerniterus is preventable.

Neonatal hyperbilirubinemia is one of the most common causes for readmission of the newborns. The need for early detection of hyperbilirubinemia in the early discharged newborns from the hospital is therefore important.

Knowledge of the neonates at risk for developing jaundice allows simple bilirubin reducing methods to be implemented before bilirubin reaches critical levels.

There are a few references which predict Neonatal hyperbilirubinemia by estimating cord blood bilirubin levels but vary in opinions.

In this present study, we assessed the Cord Serum Albumin level as a tool for screening for the risk of subsequent NH.

Sex of newborns

Table 4: Comparison of gender predilection for neonatal hyperbilirubinemia outcome in other studies.

Studies	Male	Female	p Value
Present study	98	76	0.899
Amar Taksande[8] (2005)	118	82	0.323
Rostami[9] (2005)	300	343	>0.05

In the present study, study group is uniformly distributed with 98 male and 76 female babies. There is no significant correlation (p 0.89) in the TSB levels and the sex of the newborn. Hence the present study infers that the neonatal hyperbilirubinemia (≥17mg/dl) is independent of the sex of the newborn.

Maisal, showed in a study consisting of 29934 infants, factors associated with readmission for jaundice.[10] Male sex in the study group is 74.8% compared to control with 49.6%, with p value 0.007, showing that male sex has more risk of readmission for neonatal hyperbilirubinemia.

Taksandel A, in a study on 200 neonates with 82 males and 118 females, 8 males and 11 females have serum bilirubin level of (≥17mg/dl) with p value of 0.323. So they found no correlation between the sex of the newborn and the neonatal hyperbilirubinemia (≥17mg/dl).[8]

Satrya R, showed significant correlation between the sex of the newborn and neonatal hyperbilirubinemia with p <0.05. Off 88 newborns 21 develop hyperbilirubinemia, 16 were males and 5 females.[11]

Rostami, in Iran in a study showed that there is no correlation between the neonatal hyperbilirubinemia and the sex of the newborn.[9]

Trivedi, showed, gender wise male babies have shown higher incidence of developing hyperbilirubinemia than female babies.[12] Study group consisted of 605 newborn, 305 male and 300 female. Neonatal hyperbilirubinemia developed in 115 male and 90 female.

The present study is in correlation with the study done by Amar Taksande et al, and Rostami et al.

In the present study association between the neonatal

hyperbilirubinemia and the mode of delivery was studied. 123 cases with vaginal delivery 14 developed serum bilirubin ≥17mg/dl and off 51 cases with caesarean section 6 developed significant hyperbilirubinemia (≥17mg/dl). With p value of 0.943, there is no significant association between the neonatal hyperbilirubinemia (≥17mg/dl) and the mode of the delivery.

Taksande A, in their study on 200 newborns,11 cases of 114 vaginal delivery and 8 cases of 66 caesarean section developed significant hyperbilirubinemia.[8] With p value of 0.527, showed no correlation between the mode of delivery and neonatal hyperbilirubinemia. Rostami 2005, in their study found that there is no significant association between neonatal hyperbilirubinemia and the mode of delivery.[9] Satrya R, in a study on 88 newborns, with cut off neonatal hyperbilirubinemia of ≥14.9mg/dl, showed that there is no association (p 0.885) between the mode of delivery and neonatal hyperbilirubinemia.[11]

The present study is in correlation with the other studies.

Association between the cord blood albumin level with neonatal hyperbilirubinemia (≥17mg/dl).

Table 5: Comparison of CSA level as risk indicator for NH in other studies.

Studies	Year	Total no of cases	No of case with NH	Cord albumin level correlation with NH			p value
				Group 1 (CSA level in g/dl)	Group 2 (CSA level in g/dl)	Group 3 (CSA level in g/dl)	
Sahu	2011	40	20	14(<2.8 g/dl)	6 (2.9-3.3 g/dl)	0 (>3.4 g/dl)	< 0.001
Trivedi	2013	605	205	120 (< 2.8g/dl)	59 (2.9-3.5 g/dl)	26 (>3.5 g/dl)	<0.05
Present study	2013	174	20	19(≤ 2.8g/dl)	1 (2.9-3.3g/dl)	0 (≥3.4g/dl)	<0.001

CSA=Cord Serum Albumin.
P value <0.05 is significant.

Sahu study, showed that 70% (14/20) newborn who developed significant NH had cord serum albumin level <2.8 g/dl, 30% {6/20} newborn had CSA level 2.9-3.3 g/dl and none of newborns with CSA level >3.4g/dl developed NH. There is Statistical significance noted between CSA with development of NH (p value <0.001).[13]

Trivedi, studied total of 605 newborn and 205 newborn developed significant NH in study group.[12] Study group were divided into 3 groups based on CSA levels <2.8 g/dl, 2.9-3.5g/dl, and >3.5g/dl.

In group 1, 58.35% (120/205); group 2, 28.78% (59/205) and group 3, 12.68 % (26/205) developed NH. There is statistical significance with CSA level and NH, with p value of <0.05.

In the present study, 174 newborn included and 20 newborn developed NH. The study cohort is grouped into Group 1, Group 2, Group 3, based on cord Serum Albumin level ≤2.8g/dl, 2.9-3.3g/dl and ≥3.4g/dl respectively. In group 1, 95% (19/20); Group 2, 5% (1/20) and Group 3, % developed NH requiring PT. The present study results correlated well with Shau and Trivedi study Thus CSA level appears risk indicator in predicting neonatal hyperbilirubinemia.

Hence this study indicates that CSA level ≤2.8g/dl is high risk factor for future development of NH and CSA level ≥3.4g/dl is probably safe for early discharge.

CONCLUSION

Neonatal hyperbilirubinemia occurs in 5-10% of healthy term neonates. Up to 4% of term neonates who are readmitted to the hospital during their first week of life, approximately 85% for jaundice. In the present study neonates with hyperbilirubinemia (≥17mg/dl) had significantly lower levels of cord serum albumin (≤ 2.8g/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 NH in neonates could influence decision of early discharge vs. prolonged observation. Cord serum albumin level of ≤2.8g/dl has a correlation with incidence of significant hyperbilirubinemia in term newborns. So this ≤2.8g/dl of cord serum albumin level can be used as risk indicator to predict the development of significant hyperbilirubinemia. Whereas cord serum albumin level ≥3.4g/dl is considered safe, as none of neonates developed in this group had significant hyperbilirubin.

Recommendations

The present study was done to assess the usefulness of the cord serum albumin estimation as a risk indicator to predict significant neonatal hyperbilirubinemia in a healthy term newborn who requires phototherapy subsequently.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee of J. L. N. Medical College, Ajmer, Rajasthan, India.

REFERENCES

1. Meharban Singh. Care of the Newborn. 7th ed. New Delhi: Sagar Publications; Chapter 18, Neonatal Jaundice, 2010: 254-274.
2. Cloharty JP, Stork AR, Eichenwald EC, Hansen AR. Manual of neonatal care. 7th ed, Philadelphia: Lippincott Willams and Wilkins; Chapter 26, Neonatal Hyperbilirubinemia; 2012: 304-339.
3. Radmacher P, Massey C, Adamkin D. Hiden Morbidity With Successful Early Discharge. J Perinatol. 2002;22(1):15-20.
4. Kiely M, Drum MA, Kessel W. Early discharge, risks, benefits and who decides. Clin perinatol. 1998 Sep;25(3):539-53.
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, Enzmann DR, Hahn JS, Stevenson DK. Kernicterus in a full term infant. Pediatrics. 1994 Jun 1;93(6):1003-6.
7. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term newborns. Pediatrics. 1995 Oct 1;96(4):730-3.
8. Taksande A, Vilhekar K, Jain M, Zade P, Atkari S, Verkey S. Prediction of the development of neonatal hyperbilirubinemia by increased umbilical cord blood bilirubin. Ind Medica. 2005;9(1):5-9.
9. Rostami N, Mehrabi Y. Identifying the newborns at risk for developing significant hyperbilirubinemia by measuring cord bilirubin levels. J Arab Neonatal Forum 2005;2:81-5.
10. Maisels MJ, Kring E. Length of stay, Jaundice and hospital readmission. Pediatrics.1998;101(6):995-8.
11. Rudy Satrya, Sjarif Hidayat Effendi, Dida Akhmad Gurnida. Correlation between cord blood bilirubin level and incidence of hyperbilirubinemia in term newborns. Paediatrica Indonesiana 2009;49(6):349-54.
12. Trivedi DJ, Markande DM, Vidya BU, Bhat M, Hegde PR. et al, Cord Serum bilirubin and Albumin in Neonatal Hyperbilirubinemia, Int J Int Sci Inn Tech Sec A. 2013;2(2):39-42.
13. Sahu S, Abraham R, John J, Mathew MA, Res M. Cord blood albumin as a predictor of neonatal jaundice. Int J Biol Med Res. 2011 Jan 31;2(1):436-8.

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