Original Article

To study the association between various levels of cord serum albumin (CSA) and significant neonatal hyperbilirubinemia requiring interventions like phototherapy or exchange transfusion

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Abstract

Introduction: Hyperbilirubinemia is most common normal physiological phenomenon in neonates affecting almost one third of newborn.it may lead to neuro disability leading to deafness and cerebral palsy which can be prevented if detected and treated as soon as possible. Albumin is produced in seventh week of intrauterine life and it can be measured by cord blood and in this study we can establish serum albumin with neonatal hyperbilirubinemia and can be treated by phototherapy or exchange transfusion. **Material and Method:** The study consists of 55 randomly selected eligible term neonates delivered at Rajendra Institute of Medical sciences from March 2019 to August 2020. **Conclusion:** In this study, in term neonates, level of serum albumin in umbilical cord less than 2.8 g/dl has no correlation with occurrence significant hyperbilirubinemia, so a level <2.8 gm/dl of serum albumin in umbilical cord blood can be used as critical value indicator in triaging predict the risk of occurring of significant hyperbilirubinemia in term neonates.level >3.4 gm/dl is considered safe in neonates who are the candidates for early discharge in the absence of other risk factors.

Keywords: Hyperbilirubinemia, neonate, phototherapy

Introduction

Neonatal hyperbilirubinemia (NH) (jaundice) is the most common health ailment in newborns. Unconjugated hyperbilirubinemia is a normal physiological phenomenon in most infants.[1] Clinical jaundice develops in two-thirds of all newborns. Accumulation of unconjugated bilirubin results in yellowish discoloration of skin and sclera.[1] It can result in severe neonatal jaundice if left untreated. Severe NH is an important cause of preventable neuro disability which includes deafness and cerebral palsy. Severe neonatal jaundice can cause any of the following outcome acute bilirubin encephalopathy, kernicterus or jaundice-related death.[2]

Approximately 85% of all term newborns and most of preterm infants develop clinical jaundice. Among well-term newborn, 6.1% have peak serum bilirubin greater than 12.9 mg%. A total serum bilirubin level greater than 15 mg/dl is found in 3% of normal term newborns.[2] NH is the most common among the conditions causing concern in both parents and the pediatricians.

Although American academy of Pediatric (AAP) recommend neonate to stay admitted in hospital along with mother as long as possible to make sure that there is no complication in mother

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and baby, pediatricians globally try to discharge the healthy term neonates from hospital after normal vaginal delivery as early as possible. Prevention of healthcare associated infection to reduce financial constraints to the family and religious ritual practices are the few important reasons for the early discharge.

NH is most common cause of readmission during early neonatal period (22.1%) of the babies;[3] 0.58% of the term neonates are readmitted to hospital during first week of life, among them 54.8% are for jaundice.[4]

As per recommendation by AAPs newborn discharged within 48 h medical appointment should be made within next 48 h to have a follow-up visit to look for jaundice and any other problems.[5]

Unconjugated bilirubin which is not bound to albumin can enter brain parenchyma and cause Bilirubin-induced neurological dysfunction (BIND) by apoptosis and/or necrosis.[6] BIND in healthy term babies even without hemolysis is a matter to be concerned in the early discharge of newborns.[7] It may lead to cerebral palsy, sensorineural deafness, and mental retardation.

As early discharge becoming standard of care in term newborns with no other risk factors, early identification, treatment, and prevention of BIND is becoming difficult. If initiated early, phototherapy is affordable and associated with very less complications, whereas exchange transfusion in neonates is expensive.

This limitation should be well aware of. There should be a cost effective protocol which includes screening test which can triage the neonates which are at the risk of severe NH, follow up and manage them which benefit maximum number of neonates.

Albumin can be endogenously synthesized from early fetal life in both Animals and Humans, as early as seventh week of intrauterine life.[8] In term babies, a serum albumin level of 2.8 g/dl is regarded as the lower limit[9]: mean albumin level in serum at term is 3.1 g/dl[10] and the normal range of albumin level in serum at term is 3.1 ± 3 g/dl.

Aim of the Study

The aim is to study the association between various levels of serum albumin in the umbilical cord and NH, which requires interventions such as phototherapy or exchange transfusion.

Materials and Method

This study was conducted at Rajendra Institute of Medical sciences. The study consists of 55 randomly selected eligible term neonates delivered at Rajendra Institute of Medical sciences from March 2019 to August 2020.

Research Ethics Committee of RIMS, Ranchi approved this study.

Study area: CSOT, delivery room, post-natal ward in the department obstetrics and gynaecology (RIMS) and SCNU.

Table 1: Distribution sex of neonates

Gender	No. of patients	Percentage
Male	31	56.37
Female	24	43.63
Total	55	100.0

Table 2: Distribution of mode of delivery

Mode of delivery	No. of patients	Percentage
Vaginal delivery	39	70.90
Caesarean section	16	29.09
Total	55	100.0

Table 3: Distribution of birth weight of neonates

Birth weight (kg)	No. of patients	%
2.5-3.0	35	63.64
3.0-3.5	15	27.27
>3.5	5	9.09
Total	55	100.0

Table 4: Distribution of neonate group based on level of serum albumin (g/dl) in umbilical cord blood

Cord serum albumin (gm/dl)	No. of patients	%
<2.8 (Group A)	28	50.90
2.8-3.4 (Group B)	17	30.90
>3.4 (Group C)	10	18.20
Total	55	100.0

Table 5: Distribution of neonates based on blood group

Blood group of neonate	No. of patients	%
A+	5	9.09
B+	19	34.54
AB+	4	7.27
O+	27	49.09
Total	55	100

Study population: normal healthy term newborns selected randomly after screening for exclusion criteria were included to the study.

Study design: Prospective observational study.

Study period: 18 month.

Sample size: 55 neonates.

Inclusion criteria

1. Term neonates with both sex
2. Birth weight ≥2.5 kg.
3. Delivery method (both cesarean section and vaginal delivery)
4. APGAR score at 1 min of age ≥7/10.

Exclusion criteria

Neonates presents with jaundice with 24 h of life
Preterm Neonates
Meconium stained liquor
Neonates with Rh incompatibility.
Neonatal sepsis.
Neonates with respiratory distress
Neonates born through Instrumental delivery (forceps and vacuum)
Neonates with Perinatal asphyxia.

Method of data collection

1. In this study, the parents of neonates were well explained about the purpose and nature of the study before the enrolment and written informed consent was taken.
2. Parents were interviewed to collect relevant information including demographic information using structured proforma and extracted from mother's case sheet.
3. Gestational age of neonate was estimated by Modified New Ballard score (if LMP not reliable).
4. Serum Albumin level was estimated at birth using umbilical cord blood.
5. Between 72 and 96 h after birth Total Serum Albumin level was estimated.
6. All the neonates were examined daily for first 4 postnatal days and they were assessed daily for NH and its severity.

Laboratory investigation

1. 2 ml sterile syringe was used to collect blood from umbilical cord near the placental side after its separation, and it was used to estimate the level of serum albumin in umbilical cord.
2. Venous blood samples were collected from the neonate at 72 to 96 h after birth. Blood group analysis, total and direct serum bilirubin were done using these samples.

Inference

The main outcome of this study was inferred in terms of NH.

Serumbilirubin ≥17 mg/dl after 72 h after birth was considered as hyperbilirubinemia and treatment was advised according to the guidelines by the American academy of pediatrics practice parameter, 2004.[11]

Indian Aacademy of Pediatrics—National Neonatology Forum also recommends to consider Phototherapy in neonates whose serum bilirubin levels 17 mg/dl or above after 72 h of life.[12]

Therefore, in this study, newborns with Total serum bilirubin level of ≥17 mg/dl were considered to have hyperbilirubinemia and decided that they needed intervention (like Phototherapyor Exchange Transfusion) after 72 h of age.

Table 6: Distribution of level of total serum bilirubin (mg/dl) of neonate studied

Total serum bilirubin (mg/dl)	No. of patients	%
≤10	2	3.63
10-15	37	67.27
15-17	11	20.00
≥17	6	10.90
Total	55	100

Table 7: Distribution of neonates who required phototherapy as a treatment for neonatal hyperbilirubinemia in this study

Phototherapy	No. of patients	%
No	49	89.10
Yes	6	10.90
Total	55	100

Table 8: Requirement for exchange transfusion in neonates in this study

Exchange transfusion	No. of patients	%
No	55	100
Yes	0	0
Total	55	100

Table 9: Comparison table of gender distribution and level of erum albumin in umbilical cord

Gender	Umbilical cord albumin levels (g/dl)			Total
	<2.8	2.8-3.4	>3.4	
Male	17	11	3	31
Female	11	6	7	24
Total	28	17	10	55

χ^2=3.52, *P*=0.172

Table 10: Comparison of birth weight with the level of serum albumin in the umbilical cord

Birth weight (kg)	Umbilical Cord Albumin levels			Total
	<2.8	2.8-3.4	>3.4	
2.5-3	18	13	4	35
3-3.5	8	2	5	15
>3.5	2	2	1	5
Total	28	17	10	55

χ^2=4.98, *P*=0.289

Plan for analysis

Data obtained from this study were tabulated in Microsoft Excel and subsequently analyzed using SPSS version 20.0.

Categorical variables in this study were analyzed by percentage analysis.

Simple frequency, Mean, standard deviation (SD) and median, etc., were used to analyze continuous variables and presented in tables.

Table 11: Comparison of requirement of phototherapy with umbilical cord serum albumin level

Phototherapy	Umbilical cord albumin levels			Total
	<2.8	2.8-3.4	>3.4	
No	23	16	10	49
Yes	5	1	0	6
Total	28	17	10	55

P=<0.001

Table 12: Comparison of need for exchange transfusion with level of serum albumin in umbilical cord blood

Exchange transfusion	Umbilical cord albumin levels			Total
	<2.8	2.8-3.4	>3.4	
No	28	17	10	55
Yes	0	0	0	0
Total	28	17	10	55

Table 13: Correlation of clinical variable with need for phototherapy

Variables	Phototherapy		*P*
	No (*n*=49)	Yes (*n*=6)	
Gender			
Male	28	3	0.739
Female	21	3	
Mode of delivery			
Vaginal route	35	4	0.808
Caesarean Section	14	2	
Cord blood Albumin (mg/dl)			
<2.8	23	5	<0.001
2.8-3.4	16	1	
>3.4	10	0	

For entire statistical test, applied *P* value <0.05 had been considered to reject the null hypothesis.

Observation and Results

This study was belonged to prospective observational study and it was conducted at Department of Pediatrics at Rajendra institute of medical sciences between March 2019 to August 2020 to know the relation between umbilical cord serum albumin and NH was conducted on total of 55 healthy newborns.

Table 1 depicts the distribution sex of neonates enrolled in the study; 31 (56.37%) were male, whereas 24 (43.63%) were female neonates.

Table 2 depicts the distribution of mode of delivery among the neonates in the study. Majority of the neonates in this study group were delivered by vaginal delivery which constitutes 39 out of 55 (70.90%).

The table 3 depicts distribution of weight at birth among the neonates in this study.

Among the neonates in this study group, 63.64% (n = 35) had weight at birth between 2.5 and 3.0 kg.

Mean weight at birth was 2.9 kg among the neonates in this study.

Table 4 depicts the distribution of neonates into three groups based on level of albumin measured in the umbilical cord at birth.

Group A consists of 28 newborns (50.90%).

Group B consists of 17 newborns (30.90%).

Group C consists of 10 newborns (18.2%)

Table 5 depicts the distribution of the neonates based on blood group. Majority of the neonates belong to O positive blood group, which is 49.09% (n = 27). B positive blood group was the second most common blood group in this study (34.54%) (n = 19).

Table 6 depicts the distribution level of Total Serum Bilirubin measured at 72 to 96 h of age in the neonates; 6 out of 55 newborn developed NH (serum bilirubin >17 mg/dl).

This table 7 shows that 6 out of 55 (89.10%) neonates developed NH requiring phototherapy as treatment.

Table 8 shows that none of the neonates in this study group developed NH which required exchange transfusion as treatment.

Table 9 shows the comparison of cord albumin groups with gender. No statistical significance is seen.

This comparison table 10 shows no statistical significance between cord albumin with birth weight (*P* value is >0.05).

Above table 11 shows the comparison between the neonates who developed NH requiring phototherapy and umbilical cord albumin levels. *P* value <0.001 suggests that statistical significance between two variables is present.

No statistical significance observed in the neonates in this study on comparing requirement of exchange transfusion with levels of serum albumin in umbilical cord [Table 12].

Table 13 shows the correlation of variables like sex, method of delivery, and level of serum albumin in the umbilical cord blood with neonates who developed significant NH requiring phototherapy.

Statistical significance was only seen with the levels of umbilical cord albumin ($P < 0.001$), whereas there was no statistical significance seen with variables like sex and method of delivery.

Diagnostic predictability of levels of serum albumin in umbilical cord blood for NH.

At 2.8 mg/dl, serum albumin in umbilical cord has sensitivity of 84%, specificity of 53%, positive predictive value of 18%, and negative predictive value of 90% in diagnosing NH.

If serum albumin level in umbilical cord blood <2.8 g/dl, there was 17.9% probability of occurrence of NH requiring phototherapy and with levels ≥2.8 g/dl, there is 90% chance of non-occurrence of NH requiring phototherapy.

In a similar manner, if serum albumin level in umbilical cord blood >3.4 g/dl, chance of occurrence of NH requiring phototherapy is zero.

Hence, level of serum albumin umbilical cord lesser than 2.8 g/dl can be considered as cut-off value for the occurrence of NH which require intervention. Whereas, level more than 3.4 g/dl can be regarded safe in term healthy neonates and can be discharged early.

Conclusion

In this study, in term neonates, level of serum albumin in umbilical cord less than 2.8 g/dl has no correlation with occurrence significant hyperbilirubinemia, so a level <2.8 gm/dl of serum albumin in umbilical cord blood can be used as critical value indicator in triaging o predict the risk of occurring of significant hyperbilirubinemia in term neonates. Whereas, level of serum albumin in umbilical cord more than 3.4 g/dl is regarded as safe, as no neonate with level of serum albumin >3.4 g/dl developed significant hyperbilirubinemia and a level >3.4 gm/dl is considered safe in neonates who are the candidates for early discharge in the absence of other risk factors. Hence, serum albumin level in umbilical cord can be used as an adjunct test along with transcutaneous bilirubinometry to predict the NH requiring intervention and triage the neonates for the purpose of early discharge from hospital.

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Conflicts of interest

There are no conflicts of interest.

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