Original Article

Cord blood albumin level as a predictor of neonatal physiological jaundice in healthy term neonate

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ABSTRACT

Background: Neonatal jaundice is a very common condition worldwide, occurring in up to 60% of term and 80% of pre-term newborns in the 1st week of life and the most common cause for readmission. The present study was conducted to evaluate the predictive value of umbilical cord blood albumin level for subsequent development of neonatal jaundice in healthy term neonates. The present study is conducted to find usefulness of cord blood albumin in predicting the subsequent development of significant neonatal jaundice. **Methods and Methods:** This is a hospital-based prospective study conducted in 100 healthy term neonates. Cord blood albumin level estimation was done at birth. Total serum bilirubin estimation was done for all babies with clinically suspected jaundice at 72–96 h of age. The neonates were divided into three Groups A, B, and C based on the cord albumin levels of <2.8 g/dL, 2.8–3.3 g/dL, and >3.3 g/dL, respectively. The main outcome of the study was inferred in terms of serum bilirubin ≥17 mg/dL, newborn required phototherapy, and exchange transfusion. **Results:** Groups A, B, and C had 21, 35, and 44 newborns, respectively. In Group A, 18 (85.7%) neonates had total bilirubin of >17 mg/dL, of which 16 (76.19%) required phototherapy and 2 (9.52%) needed exchange transfusion. 23 (65.7%) neonates in Group B developed jaundice, of which 12 (34.2%) needed phototherapy and none of them required exchange transfusion. In Group C, 15 (34.09%) developed jaundice of which 1 (2.2%) required phototherapy and none of them required exchange transfusion (p<0.001). **Conclusion:** Cord blood albumin level ≤2.8 g/dL is a significant risk factor for developing neonatal hyperbilirubinemia that requires early intervention, while cord blood albumin >3.3 g/dL is probably safe for early discharge. Hence, this can help to identify the at-risk neonates. Hence, routine determination of cord blood albumin level can be advocated to keep a track on at-risk neonates.

Key words: Cord blood albumin, Hyperbilirubenemia, Neonatal jaundice

Neonatal hyperbilirubinemia (NH) is the most common abnormal physical finding during the 1st week of life which affects nearly 60% of term and 80% of pre-term neonates. About 6.1% normal newborn have a serum bilirubin over 12.9 mg%. Nearly 3% of normal term newborn has serum bilirubin over 15 mg% [1]. NH is a major cause of concern for the pediatrician as well as for the parents and the most common cause for readmission (6.5% babies) during the early neonatal period [2].

Physiological hyperbilirubinemia is a result of immature liver cell, low uridine diphospho glucuronosyltransferase activity, low concentration of albumin, and increased number of erythrocytes which have a shorter life span. It is a normal response on the part of the baby due to limitations in the ability to excrete bilirubin [3].

Unconjugated bilirubin is non-polar, insoluble in water and is transported to liver bound to albumin, so amount of albumin available for binding is important. One mole of albumin binds equimolar amount of bilirubin, i.e., 1 g of albumin binds 8.5 mg of bilirubin. Bilirubin bound to albumin does not usually enter central nervous system and is thought to be non-toxic. The full-term newborn infant has a significantly lower plasma albumin level than that for adult and, correspondingly, fewer bilirubin binding sites. The albumin level is inversely correlated with gestational age, so this lack of binding sites is more pronounced in pre-term infants. Plasma albumin level increases rapidly over the first few days after birth, resulting in a mean increase over the first 7 days [4].

In India because of various reasons, early discharge has become a common practice after normal vaginal delivery as well as LSCS in the healthy term newborns. AAP recommends follow-up visit for all newborn after 48–72 h, if they are discharged early within the first 48 h of life [5]. Because of limited follow-up facilities in our country, the above recommendation is not possible resulting in delay in recognition of jaundice which might result in bilirubin-induced brain damage and serious sequelae such as cerebral palsy, sensori-neural deafness, and intellectual disability [6,7]. Neonatal hyperbilirubinemia recognition, follow-up, early treatment, and

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prevention of bilirubin-induced encephalopathy have become more difficult as a result of earlier discharge from the hospital.

Early treatment of jaundice with phototherapy is effective, simple, and cheap. Moreover, the treatment of severe neonatal hyperbilirubinemia by exchange transfusion is costly, associated with complications, time consuming, and requires skilled manpower. In India like developing countries because of limitation in neonatal intensive care unit, the ultimate aim should be early recognition and to make sure newborns gets benefited by early treatment protocol.

The concept of prediction offers an attractive option to pickup babies at risk of NH. By predicting the newborns at risk for significant neonatal hyperbilirubinemia early at birth, we can design and implement the follow-up program in these risk groups, cost effectively. The present study was conducted to find usefulness of cord blood albumin in predicting the subsequent development of significant neonatal jaundice. This helps us to decide an early discharge of the newborn in resource-limited settings.

MATERIALS AND METHODS

This is a hospital-based prospective study conducted in 100 healthy eligible term neonates. Cord serum albumin level estimation was done at birth. 3 mL of cord blood was collected at birth and was sent for estimation of cord blood albumin and TSH. Cord albumin was assessed using the biuret reaction technique using an automated analyzer. Babies were examined daily for the presence of icterus up to the 4th day. On detecting the presence of icterus, blood was sent for estimation of total bilirubin and the results were plotted on the chart to identify the type of intervention the baby required. The neonates were divided into three Groups A, B, and C based on the cord albumin levels of <2.8 g/dL, 2.8–3.3 g/dL, and >3.3 g/dL respectively. The main outcome of the study was inferred in terms of NH serum bilirubin ≥17 mg/dL, newborn required intervention, i.e., phototherapy and exchange transfusion. The inclusion criteria included term babies, both genders, mode of delivery (normal and LSCS), birth weight >2.5 kg, >7/10 at 1st and 5th min of life, and normal cord blood TSH. The exclusion criteria were pre-term, Rh incompatibility/ABO incompatibility, neonatal sepsis, instrumental delivery (forceps and vacuum), birth asphyxia, respiratory distress syndrome, meconium-stained amniotic fluid, and neonatal jaundice within 24 h of life.

All the data were entered in Microsoft excel sheet and Statistical Package for the Social Sciences version 21. Qualitative data were summarized as percentage and quantitative data were summarized as means and standard deviation. Chi-square (X^2) test was used to find the significance of difference between proportions and percentages. The mean difference of various parameters was compared using Z-test and t-test. Analysis of variance was to be used for cord blood albumin levels between groups and within groups to show if any significant difference observed. p<0.05 (<0.05) was taken as significant difference.

RESULTS

Total 100 number of newborn was taken in our study. There were 21 neonates in Group A, 35 in Group B, and 44 in Group C.

Jaundice were noted on 2nd, 3rd, and 4th postnatal day in 18, 23, and 15 neonates, respectively. The mean age of onset of jaundice in Groups A, B, and C were 3.0±0.7, 3.0±0.7, and 4.0±0.5 days, respectively. Gestational age, birth weight, and gender in Groups A, B, and C were comparable except mode of delivery (Table 1).

Table 1 shows that there was no statistically significant relation between cord blood albumin and gestational age, sex of newborns, and birth weight (p>0.05). There was statistically significant difference between cord blood albumin of babies born through normal delivery and cesarean section (p=0.001).

The incidence of jaundice in all the groups and need for intervention in the form of phototherapy and exchange transfusion is depicted in Table 2.

Table 2 shows that number of newborn who developed clinical jaundice required phototherapy and exchange transfusion in each three group is significantly differ according to the cord blood albumin level (p<0.001).

DISCUSSION

Because of increasing number of early discharged newborns, there is a corresponding danger of failing to diagnose severe hyperbilirubinemia in time. In our study, we assessed the Cord serum albumin level as a tool for screening for the risk of subsequent NH.

In our study, of 100 neonates, 85.7%, 65.7%, and 34.09% newborns developed jaundice in groups where cord blood albumin <2.5 g/dL, 2.5–3.3 g/dL, and >3.3 g/dL, respectively (p<0.001). In Group A, 76.19% required phototherapy and 9.52% required exchange transfusion. In Group B, 34.2% required phototherapy and no one required exchange transfusion, while in Group C, only 2.2% required phototherapy and none of them required exchange transfusion (p<0.001).

The age of onset of jaundice in our study in majority of neonates was on 3rd postnatal day. Other workers in their studies also noticed the onset of jaundice on 3rd and 4th postnatal in majority of neonates. Anand and Magotra found that 45.7% neonates had onset of jaundice on 3rd postnatal day followed by 35.3% neonates on 4th postnatal day [12]. Sethi *et al*. reported development of jaundice on 3rd postnatal day of life in two-third newborns [13].

The present study infers that the NH (≥17 mg/dL) is independent of the sex of the newborn (>0.05). Taksande *et al*. [14] in a study on 200 neonates and Rostami and Mehrabi [15] study done in Iran found no correlation between the sex of the newborn and the NH (≥17 mg/dL).

In the present study, the association between the NH and the mode of delivery was studied. Neonatal hyperbilirubinemia was noted to be high in babies delivered through LSCS (0.001). Taksande *et al*. study [14] showed no correlation between the mode of delivery and NH with p=0.527.

Our study had few limitations such as, only full term healthy neonates were enrolled in this study and follow-up was done only for 4 days for the rise in bilirubin. Table 3 shows the results of other studies on similar topic..

Table 1: Basic demographic characteristics of all three groups

Basic demographic characteristics	Group A (n=21) (cord blood albumin<2.8 g/dL)	Group B (n=35) (cord blood albumin 2.8–3.3 g/dL)	Group C (n=44) (cord blood albumin>3.3 g/dL)	p
Gestational age (weeks)	38.1±0.7	37.9±0.8	37.8±0.7	>0.05
Birth weight (kg)	2.5±0.6	2.8±0.4	2.8±0.8	>0.05
Gender, n (%)				
Male	13 (60)	20 (55)	23 (52)	>0.05
Female	8 (40)	15 (45)	21 (48)	
Mode of delivery, n (%)				
Cesarean section	10 (47)	24 (68)	13 (30)	0.001
Normal delivery	11 (52)	11 (32)	31 (70)	

Table 2: Incidence of clinical jaundice and requirement of phototherapy or exchange transfusion in three groups

Incidence of clinical jaundice and requirement of interventions	Group A (n=21) (cord blood albumin<2.8 g/dL), n (%)	Group B (n=35) (cord blood albumin 2.8–3.3 g/dL), n (%)	Group C (n=44) (cord blood albumin>3.3 g/dL), n (%)	p
Neonates developed clinical jaundice (Kramer≥3)	18 (85.7)	23 (65.7)	15 (34.09)	<0.001
Newborns requiring phototherapy	16 (76.19)	12 (34.2)	1 (2.2)	<0.001
Newborns requiring exchange transfusion	2 (9.52)	0	0	

Table 3: Cord blood albumin level as a risk indicator of neonatal hyperbilirubinemia in some studies

Author	Total number of NNH	Cord blood albumin correlation with NNH			p
		<2.8 mg/dL, n (%)	2.8–3.3 mg/dL, n (%)	>3.3 mg/dL, n (%)	
Sahu *et al.*[8]	20	14 (70)	6 (30)	0	<0.001
Trivedi *et al.*[9]	205	120 (58)	59 (28)	26 (12.6)	<0.05
Aiyappa *et al.*[10]	72	44 (61)	28 (39)	0	<0.0005
Sayed *et al.*[11]	64	17 (26)	34 (53.1)	13 (20.3)	<0.001

NNH: Neonatal hyperbilirubinemia

CONCLUSION

Umbilical cord serum albumin levels are useful in prediction of subsequent development of significant neonatal jaundice in healthy term newborns. Neonates with umbilical cord blood albumin level more than 3.3 g/dL can be safely discharged early whereas neonates with albumin levels <3.3 g/dL will need a close follow-up to check for development of jaundice. Hence, we recommended that routine estimation of cord blood albumin should be emphasized in all term newborns in institutional delivery. It will help to design and implement the follow-up program in high-risk groups effectively and to plan early discharge of babies and mothers.

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