

ORIGINAL ARTICLE

UTILITY OF CORD BLOOD ALBUMIN AS A PREDICTOR OF SIGNIFICANT NEONATAL JAUNDICE IN HEALTHY TERM NEWBORNS

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Abstract

Aim: To study the association between cord blood albumin level and subsequent development of significant neonatal jaundice (NNJ) in healthy term newborns.

Methods and Materials: A prospective study was done in 100 sequentially born healthy term babies (gestational age > 37 weeks) of either gender, from any mode of delivery, with any birth weight, Apgar score ≥ 7 at first and fifth minutes of life, without ABO and Rh incompatibility. They were divided into 3 groups A, B, and C according to cord blood albumin levels < 2.8 gm/dl, 2.8-3.3 gm/dl and >3.3 gm/dl respectively and then followed clinically for jaundice upto day 5 of life or till hospital stay whichever was later. Wherever necessary further laboratory tests were done and baby managed accordingly.

Results: Group A, B, and C had 22, 34, and 44 newborns respectively. In group A, 21 (95.5%) neonates developed jaundice, of which 18 (81.8%) required phototherapy and 2 (9.1%) needed exchange transfusion; whereas 27 (79.4%) neonates in group B developed jaundice, of which 9 (26.6%) needed phototherapy and none required exchange transfusion. In group C 16 (36.6%) developed jaundice of which 1 (2.4%) required phototherapy and none of them required exchange transfusion (p value <0.001).

Conclusion: Umbilical cord serum albumin levels are useful in predicting subsequent neonatal jaundice in healthy term newborns. Neonates with cord blood albumin levels > 3.3 gm/dl are probably safe for early discharge whereas neonates with albumin levels <3.3 gm/dl will need a close follow up to check for development of jaundice.

Keywords: neonatal jaundice, cord blood albumin, hyperbilirubinemia, kernicterus.

Introduction

Clinical jaundice is seen in 60-70% of term and about 80% of preterm newborns. (1) Over 6.1% of well term newborns have a serum bilirubin over 12.9 mg%. Serum bilirubin over 15 mg% is found in 3% of normal term newborns. (1) 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 early naming ceremony and also due to economical constraints. American Academic of Pediatrics (AAP) recommends that newborns discharged within 48 hours should have a follow-up visit after 48 to 72 hours for any significant jaundice and other problems. (2) This recommendation is not appropriate for our country like India due to limited follow-up facilities in the community. These babies may develop jaundice which may be over-looked or there may be delay in recognition unless the baby is closely monitored.

Concern to the pediatrician regarding early discharge are reports of bilirubin induced brain damage

in healthy term infants even without hemolysis. Though exact serum bilirubin level that leads to development of kernicterus in icteric newborn is not known, serum bilirubin level more than 20 mg/dl is likely to be toxic and may cause significant damage to brain. (1) The concept of prediction of jaundice offers an attractive option to pick up babies at risk of neonatal hyperbilirubinemia. Visual assessment of serum total bilirubin (STB) levels as suggested by Kramer (3) relies on the cephalocaudal progression of jaundice with a rising STB level (head and neck, 4 to 8 mg/dl [68 to 292 $\mu\text{mol/l}$]; upper trunk, 5 to 12 mg/dl [86 to 205 $\mu\text{mol/l}$]; lower trunk and thighs, 8 to 16 mg/dl [137 to 274 $\mu\text{mol/l}$]; palms and soles, greater than 15 mg/dl [257 $\mu\text{mol/l}$]), is now known to be fraught with error. There is also considerable inter-laboratory variation among STB levels measured at different laboratories. (4) Albumin helps in hepatic transportation of bilirubin and its clearance. Low serum albumin level will decrease bilirubin clearance and thus will increase significant hyperbilirubinemia. There is paucity of studies on cord blood albumin as a predictor of severity of neonatal jaundice. (5-7) Hence the present study was conducted to determine whether cord blood albumin helps in predicting subsequent development of neonatal jaundice that requires interventions like phototherapy or exchange transfusion.

Methods & Materials

This prospective study was carried out at neonatal unit, Mahila Chikitsalaya after approval of the institute ethics committee of the SMS Medical College & Hospital, Jaipur. Total 100 sequentially born healthy term babies (gestational age > 37 weeks) of either gender, from any mode of delivery, with any birth weight, Apgar score ≥ 7 at first and fifth minutes of life, without ABO and Rh incompatibility were included in the study. The relevant history of mother and baby was taken and thorough physical and clinical examination of all the neonates was performed. Two ml of cord blood was collected during delivery in two plain vials and send to laboratory for baby's blood group and estimation of serum albumin, by BCG (bromocresol green colorimetric) auto analyzer method.

These neonates were divided in three groups A, B, and C according to cord serum albumin levels < 2.8 gm/dl, 2.8 - 3.3 gm/dl and > 3.3 gm/dl respectively. Weight of the newborn was recorded and gestational age was calculated by last menstrual period, or by New Ballard score. They were followed up daily for development of jaundice, sepsis or any other illness till 5th day of life or hospital stay whichever was later as serum bilirubin reaches its peak levels between 3rd to 5th day in healthy term newborns. (8) Those suspected to have jaundice of zone ≥ 3 according to Kramer dermal chart, (3) were tested for serum bilirubin level by Micro lab Semiautomatic Analyzer based on the method of Jendrassik and Grof using venous blood. Wherever necessary, further other relevant blood investigations were done.

The main outcome of the study was inferred in terms of significant hyperbilirubinemia which needed phototherapy or exchange transfusion (ET). The neonates who required no intervention or phototherapy and or exchange transfusion for management of hyperbilirubinemia from three groups were noted.

All data collected were entered in excel sheet to prepare master chart. Qualitative data was summarised as percentage and quantitative data was summarised as means and standard deviation. Chi-square (X2) test was used to find out the significance of difference between proportions & percentages. The mean difference of various parameters was compared by using Z-test and t-test. ANOVA was used for cord blood albumin levels between groups and within groups to show if any significant difference observed. 'P' value less than 0.05 (<0.05) was taken as significant difference.

Results

There were 24 neonates in Group A, 34 in Group B and 44 in Group C. Fifty-three (53%) newborns were born of primigravida mothers and 28 (28%) were born to second gravid mother. The age of onset of jaundice were noted on 2nd, 3rd, and 4th postnatal day in 27, 52 and 21 neonates respectively. The mean age of onset of jaundice in Group A, B, and C were 3.0 ± 0.7, 3.0 ± 0.7, and 3.2 ± 0.7 days respectively. Demographic characteristics were comparable in all three groups except mode of delivery (Table 1). The incidence of jaundice in all the groups and need for intervention in form of phototherapy and exchange transfusion is depicted in Table 2.

Discussion

Unconjugated bilirubin is non-polar, insoluble in

Table 1: Basic demographic characteristics of all three groups

		Group A (n=22) (Cord blood albumin <2.8gm/dl)	Group B (n=34)(Cord blood albumin 2.8-3.3gm/dl)	Group C (n=44) (Cord blood albumin >3.3gm/dl)	P value
Gestational age (months)		38.1 ± 0.9	37.9 ± 0.8	37.9 ± 0.7	> 0.05
Birth weight (kg)		2.8 ± 0.4	2.8 ± 0.4	2.8 ± 0.4	> 0.05
Gender	M	13 (60%)	19 (55%)	23 (52%)	> 0.05
	F	9 (40%)	15 (45%)	21 (48%)	
Caesarean section		10 (46%)	24 (70%)	13 (30%)	0.001
Mode of feeding	B	19 (86%)	26 (77%)	32 (73%)	0.07
	B+T	3 (14%)	8 (23%)	12 (27%)	
Oxytocin induced labour		4 (18%)	4 (12%)	8 (18%)	0.41

Note: M-Male; F-Female; B-Breast fed; B+T-Breast + Top fed

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

	Group A (n=22) (Cord blood albumin <2.8gm/dl)	Group B (n=34) (Cord blood albumin 2.8-3.3gm/dl)	Group C (n=44) (Cord blood albumin >3.3gm/dl)	P-value
Neonates developing clinical jaundice; kramer dermal zone > 3	21 (95.5%)	27(79.4%)	16 (36.6%)	< 0.001
Newborns requiring phototherapy	18 (81.8%)	09 (26.6%)	01 (2.4%)	< 0.001
Newborns requiring exchange transfusion	02 (9.1%)	0	0	

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. one gram of albumin bind 8.5 mg of bilirubin. (1) 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 preterm infants. Plasma albumin level increases rapidly over the first few days after birth, resulting in a mean increase over the first 7 days of almost 30%. Adult level is reached by about 5 months of age. (9) Normal ranges of serum albumin in different age groups are 0-4 days = 2.8-4.4 gm/dl, 4 days - 14 years = 3.8-5.4 gm/dl, adults = 3.5-5.2 gm/dl and > 60 year = 3.2-4.6 gm/dl.

The current AAP guidelines (2) for managing healthy jaundiced term and near-term newborns recommends the use of the total bilirubin concentration/albumin (TBC/A) ratio in addition to the TBC. (10) While the ratio is a rough measure of bilirubin-albumin binding and has not been widely used clinically, clinicians are encouraged to measure the albumin level along with the TBC. (11,12) However, a lower than expected albumin at least alerts the physician to the possible need for intervention at lower than usual TBC levels. Both the AAP (2) and National Institute of Child Health and Human Development (NICHD) (13) have called for further research into the clinical use of bilirubin-albumin binding to improve our ability to determine those babies that truly needed treatment.

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 et al, found that 45.7% neonates had onset of jaundice on 3rd postnatal day followed 35.3% neonates on 4th postnatal day. (14) Sethi et al, reported development of jaundice on 3rd postnatal day of life in two-third newborns. (15) This supports the observation that non-hemolytic jaundice in term babies appears mostly on 3rd day of life because of increase production of bilirubin, delayed maturation of liver enzymes and increased entero-hepatic circulation. (2)

In our study out of 100 neonates 95.5%, 79.4%, 36.4% newborns developed jaundice in group A, B, and C respectively. In group A, 81.8% required phototherapy and 9.1% required exchange transfusion. In group B 26.5% required phototherapy and no one required exchange transfusion, while in group C only 2.3% required phototherapy and none of them requiring exchange transfusion. Similarly Suchanda et al, in a study on 40 newborns found that 82% of neonates who had albumin levels less than 2.8 gm/dl developed hyperbilirubinemia requiring phototherapy and about 12% needed exchange transfusion. At higher levels of albumin that is 2.8 - 3.3 gm/dl, 40% needed phototherapy and with cord blood albumin > 3.3 gm/dl, none of the neonates needed any intervention

for hyperbilirubinemia. (7) Similarly in study by Trivedi et al, on 605 infants, 205 babies developed hyperbilirubinemia of which 120 (58.5%) babies had cord serum albumin level < 2.8gm/dl, 59 (28.8%) babies had cord serum albumin level in the range of 2.8 - 3.5 gm/dl, whereas 26 (12.7%) babies developed hyperbilirubinemia even though cord serum albumin level was more than 3.5 gm/dl. (p <0.05) (6) It is already known that some studies favour that estimation of cord blood bilirubin could predict subsequent hyperbilirubinemia, (16,17) whereas others disagreed of it, (18) hence we planned to study cord blood albumin as a predictor of subsequent NNJ.

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 gm/dl can be safely discharged early whereas neonates with albumin levels <3.3 gm/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 programme in high risk groups effectively, and to plan early discharge of babies and mothers.

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Conflict of Interest: None

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