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A COMPARISON STUDY: CORD SERUM ALBUMIN IS COMPARED WITH CORD SERUM BILIRUBIN AS A RISK INDICATOR IN PREDICTING NEONATAL JAUNDICE

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ABSTRACT: OBJECTIVE: 1. Comparing Cord Serum Albumin level (CSA) with Cord Serum Bilirubin (CSB) in predicting neonatal hyperbilirubinemia. 2. To know the sensitivity, specificity, Positive predictive value and negative predictive value of CSA and CSB in predicting neonatal jaundice in term neonates. **METHOD:** Prospective study was performed on 174 healthy term neonates. Relevant maternal history is collected. Cord blood was collected from the healthy term neonates at birth, CSA and CSB measured. Neonate was assessed clinically every day. Total Serum Bilirubin (TSB) and blood group were assessed in neonate during 72-96 hours of life. TSB value ≥17mg/dl is considered Neonatal Hyperbilirubinemia (NH) which requires intervention like phototherapy (PT) or Exchange transfusion (ExT). **RESULT:** Study cohort is grouped in Group 1, Group 2 and Group 3 based on Cord Serum Albumin level ≤2.8g/dl, 2.9-3.3g/dl and ≥3.4g/dl, respectively. Based on CSB, study cohort divided into neonates with CSB ≤ 2mg/dl and CSB ≥ 2.1mg/dl. Statistical analysis done for correlation of CSA and CSB with NH. Statistical significance is seen for both CSA and CSB. **CONCLUSION:** Both CSA and CSB are equally effective in predicting NH at birth. These study variables can be considered as neonatal screening tool for NH for term neonates.
KEYWORDS: Cord Serum Albumin; Cord Serum Bilirubin; Neonatal Hyperbilirubinemia; Prediction; Neonates.

INTRODUCTION: During the neonatal period, metabolism of bilirubin is in transition from the fetal stage to the adult stage[1]. Uridine diphosphoglucuronyl transferase (UDPGT) important liver enzyme for conjugation and excretion of bilirubin is detectable at 18 – 20 weeks of gestation. UDPGT levels in full term neonates are usually less than 0.1% of adult values. Adult value of this enzyme activity is demonstrable only by 6–14 weeks of postnatal life[2].

Synthesis of albumin appears at approximately the 7th-8th wk. in the human fetus and increases in inverse proportion to that of α-fetoprotein. Albumin concentrations are low in a neonate (~2.5 g/dL), reaching adult levels (~3.5 g/dL) after several months.[3]

Albumin has been described as "the body's tramp steamer, shuttling cargo of various kinds between ports of call". Its load includes bilirubin, free fatty acids, calcium, etc.[4]

Bilirubin binds to albumin in an equimolar ratio. Free bilirubin is anticipated when the bilirubin- to- albumin (B: A) ratio is > 0.8. Around 8.5mg of bilirubin will bind tightly to 1 g of albumin.[3]

Neonatal Hyperbilirubinemia (NH) is commonest abnormal physical finding during the first week of life. Serum bilirubin over 15 mg% is found in 3% of normal term neonates.[3] Neonatal Hyperbilirubinemia (NH) is the most common cause for readmission during the early neonatal period (6.5%).[5] American Academy of Pediatrics (AAP) recommends that neonate discharged within 48

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hours should have a follow-up visit after 48 to 72 hours for any significant jaundice and other problems.[6] This recommendation is not appropriate for our country due to poor access to health care facility. NH which may be over looked or delay in recognition by parents, because lack of knowledge. Concern of pediatrician regarding the early discharge is bilirubin encephalopathy sequel occurring in healthy term infants even without hemolysis. [7, 8] Physical examination is not a reliable measure of the serum bilirubin. By predicting the neonates at risk for significant NH early at birth, we can design and implement the follow-up programme in these risk groups, cost effectively.

There are studies to predict NH by measuring cord albumin and cord bilirubin individually. The present study is carried out comparing these two variables.

Hence the objectives of the study are:

1. Comparing Cord Serum Albumin level (CSA) with Cord Serum Bilirubin (CSB) in predicting neonatal hyperbilirubinemia.
2. To know the sensitivity, specificity, Positive predictive value and negative predictive value of CSA and CSB in predicting neonatal jaundice in term neonates.

METHODS AND MATERIALS: This prospective study was conducted in Adichunchanagiri Institute of Medical sciences. The study cohort consists of 174 randomly selected eligible term neonates delivered at our hospital from December 1st 2011 to May 31st 2013.

Inclusion criteria: Term babies both genders, Mode of delivery (normal and C-section), Birth weight ≥2.5kg, and APGAR ≥7/10 at 1 min.

Exclusion criteria: Preterm, Rh incompatibility, Neonatal sepsis, Instrumental delivery (forceps and vacuum), Birth asphyxia, Respiratory distress, Meconium stained amniotic fluid, and Neonatal jaundice within 24 Hours of life.

Demographic profile and relevant maternal information was collected by interviewing the mother and from mother's case sheet. Cord blood of 2 ml was collected during the delivery from placental end and sent for analysis. Gestational age was assessed by New Ballard score. All the babies were followed up daily for first 4 postnatal days and babies were daily assessed for NH and its severity. Total Serum Bilirubin (TSB) estimation was done at 72-96 hours of age for all neonates.

Cord blood collected at birth was analyzed by auto analyzer method (Erba EM 200) for Cord Serum Albumin and Cord Serum Bilirubin estimation.

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.

RESULTS: Data collected were analyzed using appropriate statistical software like namely SAS 9.2, SPSS 15.0.

Study group was divided based on cord serum albumin level in to 3 groups (Table I).

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Cord Serum Albumin (g/dl)	No. of patients	%
≤2.8 (Group 1)	81	46.5
2.9-3.3 (Group 2)	53	30.5
≥3.4 (Group 3)	40	23.0
Table I: Grouped based on Cord Serum Albumin (g/dl) level		

Study group divided based on cord serum bilirubin in two (Table II).

Cord bilirubin (mg/dl)	No. of Neonates	%
≤2	94	54.0
≥2.1	80	46.0
Total	**174**	**100.0**
Table II: Grouped based on Cord Serum Bilirubin (mg/dl) level		

The Demographic variables and the variables which influence the neonatal hyperbilirubinemia directly or indirectly were compared and shown in table III.

Variables	Neonatal Hyperbilirubinemia		P value
	No (n=154)	Yes (n=20)	
Gender			
• Male	87(56.5%)	11(55%)	0.899
• Female	67(43.5%)	9(45%)	
Mode of delivery			
• Cesarean Section	45(29.2%)	6(30%)	0.943
• Vaginal route	109(70.8%)	14(70%)	
Oxytocin drug use			
• No	60(39%)	9(45%)	0.603
• Yes	94(61%)	11(55%)	
Card Serum Albumin (mg/dl)			
• ≤2.8	58(37.7%)	19(95%)	<0.001**
• 2.9-3.3	56(36.4%)	1(5%)	
• ≥3.4	40(26%)	0(0%)	

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ABO Incompatibility			
• No	151(98.1%)	19(95.0%)	0.389
• Yes	3(1.9%)	1(5.0%)	
Cord Serum Bilirubin(mg/dl)			
• ≤ 2	94(61%)	0(0%)	<0.001**
• ≥2.1	60(39%)	20(100%)	
Table III: Correlation of Clinical Variable with Neonatal hyperbilirubinemia			

** P value <0.05 is considered significant.

In table IV, the diagnostical correlation of cord serum albumin and cord serum bilirubin is compared with neonatal hyperbilirubinemia.

	Sensitivity	Specificity	PPV	NPV
Cord serum Albumin level ≤2.8	95.00	62.34	24.68	98.97
Cord serum bilirubin level ≥2.1	100.00	61.04	25.00	100.00
Table IV				

Sensitivity: probability that a test result will be positive when the disease is present (true positive rate).
Specificity: probability that a test result will be negative when the disease is not present (true negative rate).
Positive predictive value: probability that the disease is present when the test is positive.
Negative predictive value: probability that the disease is not present when the test is negative

DISCUSSION: Incidence of hyperbilirubinemia varies from 8.3% to 12.8%.[9,10] Incidence of hyperbilirubinemia in our study is 11.5% which correlates with other studies.

The study cohort consisted of 98 male and 76 female babies. The neonatal hyperbilirubinemia (≥ 17mg/dl) is independent of the sex of the neonate. Amar Taksande et al study on 200 neonates with 82 males and 118 females found no correlation between the sex of the neonate and the neonatal hyperbilirubinemia (≥17mg/dl).[11]

In our study, there is no significant association (p >0.05) between the neonate born to mother who received oxytocin and neonatal hyperbilirubinemia. Out of 174, only 105 received oxytocin for induction of labor. NH developed in 11/105 neonates whose mothers received oxytocin.

Oral E et al 2003, in their study regarding effect of oxytocin on NH, concluded no significant effect of oxytocin infusion on neonatal hyperbilirubinemia unless it was for the augmentation of labour.[12]

Amar Taksande et al in his study showed no significant association (p 0.245) between the Oxytocin induction of labor and neonatal hyperbilirubinemia.[10]

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Our study result is similar with the studies of Oral E et al and Amar Taksande et al regarding oxytocin effect on neonatal hyperbilirubinemia.

Sahu et al study, 2011, showed that 70% (14/20) neonate who developed significant NH had cord serum albumin level < 2.8 g/dl, 30% (6/20) neonate had CSA level 2.9-3.3 g/dl and none of neonates with CSA level ≥3.4g/dl developed NH. There is Statistical significance noted between CSA with development of NH (p value <0.001).[13]

In our study, 174 neonates included and 20 neonate developed NH. The study cohort are 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, 0 % developed NH requiring PT.

Our study results correlated well with Shau et al.

Trivedi et al, studied correlation of cord serum albumin level with cord serum bilirubin to predict the risk for hyperbilirubinemia in term newborns. 33.88% babies developed significant NH. Babies with cord serum bilirubin >2.0mg/dl, 76.3% developed significant NH in first seven day of the life. Among 33.88% babies who developed significant NH, 53.53% babies had cord serum albumin ≤ 2.8g/dl. This study concluded that cord serum albumin gives additional clue in visualizing future significant NH[14].

In our study, 11.5% (20/174) developed NH, among these 95% (19/20) had cord serum albumin ≤2.8g/dl and 100% (20/20) had a cord serum bilirubin level ≥2.1mg/dl.

At cord serum albumin level ≤2.8g/dl, sensitivity, specificity and NPV are 95%, 62.34% and 98.97% respectively, for predicting NH at birth. Similarly at cord serum bilirubin level ≥2.1mg/dl, 100%, 61.04% and 100% are sensitivity, specificity and NPV respectively for predicting NH. Hence these values can be considered as critical values in predicting NH at birth.

Cord serum albumin level ≥3.4g/dl with cord serum bilirubin level ≤ 2mg/dl are considered safe, as none of neonates developed in this group had significant hyperbilirubinemia.

Limitations of the study are, only full term healthy neonates were taken for the study, sample size is less and require further study with large sample is required.

CONCLUSION: There is a correlation between Cord serum albumin level, cord serum bilirubin and neonatal hyperbilirubinemia in healthy term neonates. Hence both the study variable cord serum albumin and cord serum bilirubin are equally effective in predicting neonatal hyperbilirubinemia at birth. These variables can be used as screening test for neonatal hyperbilirubinemia for term neonates and is cost effective in individualizing the follow-up and planning for early discharge.

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