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Original Research Article

A study to determine the level of cord blood albumin in predicting neonatal jaundice

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ABSTRACT

Background: Most unconjugated bilirubin formed by the fetus is cleared by the placenta into the maternal circulation. Albumin constitutes 70 - 75% of Plasma oncotic pressure. Another important function of albumin is its antioxidant property. Bilirubin binds to albumin in an equimolar ratio. Free bilirubin is anticipated when the molar bilirubin- to- albumin (B: A) ratio is >0.8 Objective of the study was to predict the proportion of newborn requiring intervention for NH (phototherapy or exchange transfusion) based on cord serum albumin level at birth.
Methods: The present prospective study was conducted at Navodaya Medical College, Raichur from October 2018 to November 2019. A total of 180 babies which were born during the study period were included in the study. INCLUSION CRITERIA• Term babies both genders• Mode of delivery (normal and C-section)• Birth weight ≥2.5kg.• APGAR ≥7/10 at 1 min. 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 were daily assessed for NH and its severity.
Results: In our study nearly 54.4% of them had Cord Serum Albumin levels of less than 2.8 gm/dl, 27.3% of them had albumin levels of 2.9 to 3.3 gm/dl, 18.3% of them had Serum Albumin of 3.4 gm/dl. Out of 180 study subjects, 13.9% of them required phototherapy to treat neonatal hyper bilirubinemia and 2.8% of the study subjects required exchange transfusion.
Conclusions: From the present study, 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.

Keywords: Bilirubin, Albumin, Jaundice, Neonate, Predictor

INTRODUCTION

Jaundice is a well-known clinical entity in the Indian Medicine (Ayurveda). Since the Vedic Era (1500 BC - 800 BC) this disease has been described. Jaundice has been mentioned among diseases in Atharvaveda. Ayurveda is based on "Tridosha theory of disease" - Vata (wind), Pitta (gall) and Kapha (mucus). Charaka Samhita (200AD) described one of the first references to skin icterus. Jaundice (kamale) is a specific condition, which arises due to aggravation of bile.[1]

Most unconjugated bilirubin formed by the fetus is cleared by the placenta into the maternal circulation. Formation of conjugated bilirubin is limited in the fetus because of decreased fetal hepatic blood flow, decreased hepatic ligandin and decreased UDPG-T activity. Uridine diphosphoglucuronyl transferase (UDPGT) is detectable at 18 - 20 weeks. UDPGT levels in full term and preterm 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]

Bilirubin is detected in normal amniotic fluid as early as 12 weeks of gestation, but usually disappears by 36-37 weeks.[3] During the neonatal period, metabolism of bilirubin is in transition from the fetal stage during which the placenta is the principal route of elimination of the lipid soluble, unconjugated bilirubin to the adult stage, during which the water-soluble conjugated form is excreted from hepatic cells into the biliary system and gastrointestinal tract.[4]

Bilirubin is derived from the breakdown of heme containing protein in the reticuloendothelial system.

- The major heme containing protein is red blood cell hemoglobin. This is the source of 75% of all bilirubin production.
- The other 25% of bilirubin is called early labeled bilirubin. It is derived from hemoglobin released by ineffective erythropoiesis in the bone marrow, from other heme containing proteins in tissues (ex: myoglobin, cytochromes, catalase, peroxidase) and from free heme.[5]

Albumin (69 kDa) is the major protein of human plasma and makes up approximately 60% of the total plasma protein. About 40% of albumin is present in the plasma, and the other 60% is present in the extracellular space.

Synthesis of albumin appears at approximately the 7th-8th wk in the human fetus and increases in inverse proportion to that of α-fetoprotein, which is the dominant fetal protein. Albumin concentrations are low in a neonate (<2.5 g/dL), reaching adult levels (>3.5 g/dL) after several months.[4]

Albumin constitutes 70 - 75% of Plasma oncotic pressure. Albumin has been described as "the body's tramp steamer, shuttling cargo of various kinds between ports of call". Its load includes bilirubin, cysteine, free fatty acids, calcium, and drugs. Another important function of albumin is its antioxidant property. Serum albumin is frequently utilized as an index of the hepatocyte's ability to carry out synthetic function. Because the half-life of albumin is 19-21 days, serum albumin may not reflect acute changes in liver synthetic ability.[3]

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

The 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 programmer in these risk groups, cost effectively.

Objective of the study was to predict the proportion of newborn requiring intervention for NH (phototherapy or exchange transfusion) based on cord serum albumin level at birth.

METHODS

The present prospective study was conducted at Navodaya Medical College, Raichur from October 2018 to November 2019. A total of 180 babies which were born during the study period were included in the study.

Inclusion criteria

- Term babies both genders
- Mode of delivery (normal and C-section)
- Birth weight ≥2.5kg.
- 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.
- Neonatal jaundice within 24 Hours of life.

Demographic profile and relevant information was collected by using structured Preformat 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 were daily assessed for NH and its severity.

Laboratory investigation

- Cord blood (2ml) was collected from placental side after its separation and subjected to investigation:
  - Cord Serum Albumin level
- Venous blood samples were collected from the baby at 72 to 96 hours of life. These samples were subjected to following investigation
  - Total and direct serum bilirubin.
  - Blood group analysis.

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.

RESULTS

A total of 180 newborn study subjects who met the inclusion criteria were included in the study. In the present study nearly 58.3% of the subjects were male and 41.7% of the newborn were female. Nearly 62.2% of the neonates included in the study were from rural areas and 37.8% from urban areas. Nearly 75.5% of them were born by normal vaginal delivery. The newborns weighing between 2.5 to 3 kg was found to be 66.1%, between 3 to 3.5 kg was 21.1% and more than 3.5 kg was 12.8% (Table1).

Table 1: Social Profile of the study subjects.

Social profile		Frequency	%
Gender	Male	105	58.3
	Female	75	41.7
Place	Rural	112	62.2
	Urban	68	37.8
Mode of Delivery	Normal	136	75.5
	LSCS	44	24.5
Birth Weight	2.5 to 3.0 kg	119	66.1
	3.0 to 3.5 kg	38	21.1
	>3.5 kg	23	12.8

Table 2: Distribution of laboratory investigations and treatment of study subjects.

Laboratory investigations		Frequency	%
Cord serum albumin levels (gm/dl)	<2.8	98	54.4
	2.9-3.3	49	27.3
	>3.4	33	18.3
Total serum bilirubin (mg/dl)	<10	12	6.7
	10-14	132	73.3
	15-17	11	6.1
	>17	25	13.9
Phototherapy	Yes	25	13.9
	No	155	86.1
Exchange transfusion	Yes	5	2.8
	No	175	97.2

In present study nearly 54.4% of them had Cord Serum Albumin levels of less than 2.8 gm/dl, 27.3% of them had albumin levels of 2.9 to 3.3 gm/dl, 18.3% of them had Serum Albumin of 3.4 gm/dl. The total Serum Bilirubin was found to more than 10 mg/dl in 6.7%, 10 to 14 mg/dl in 73.3%, 15 to 17 mg/dl in 6.1%, and more than 17 mg/dl in 13.9 % of the study subjects. Out of 180 study subjects, 13.9% of them required phototherapy to treat neonatal hyper bilirubinemia and 2.8% of the study subjects required exchange transfusion (Table 2).

Among 25 study subjects who underwent phototherapy nearly 20 of them had albumin level less than 2.8 gm/dl and 5 subjects had albumin levels of 2.9 to 3.3 gm/dl. All the 5 cases which underwent exchange transfusion had albumin levels of less than 2.8gm/dl (Table 3).

Table 3: Comparison of phototherapy and exchange transfusion with cord serum albumin.

Treatment required		Cord serum albumin levels (gm/dl)		
		<2.8	2.9 to 3.3	> 3.4
Phototherapy	Yes	20 (20.4%)	5 (10.2%)	0 (0%)
	No	78 (79.6%)	44 (89.8%)	33 (100%)
Exchange transfusion	Yes	5 (5.1%)	0 (0%)	0 (0%)
	No	93 (94.9%)	49 (100%)	33 (100%)

The diagnostic predictability of cord serum albumin level of less than 2.8 gm/dl the sensitivity was found to be 96.5%, Specificity was 65.5%, Positive Predictive Value was 32.1%, Negative predictive Value was 99.8% and diagnostic Accuracy was 69.4% (Table 4).

Table 4: Diagnostic predictability of cord serum albumin levels (<2.8 gm/dl) for neonatal hyperbilirubinemia.

Diagnostic predictability of cord serum albumin levels (<2.8 gm/dl)	
Sensitivity	96.5 %
Specificity	65.5%
PPV	32.1%
NPV	99.8%
Diagnostic accuracy	69.4%

DISCUSSION

The presence of Neonatal Hyperbilirubinemia is considered to be one of the most common causes for the newborn to get admission to the hospital. The early diagnosis and any tool to predict the presence of hyperbilirubinemia among the newborn will be helpful in reducing the chances of hospital readmission due to physiological causes.

It was found that the gender of child is not related to the presence of neonatal hyperbilirubinemia. Similar study conducted by Maisal et al, and Amar Taksande et al,

also opined and found that the gender of the child is independent to the occurrence of Neonatal Hyperbilirubinemia.[6,7] The study findings of Trivedi et al, was found to be contrasting to our study findings where male babies had shown higher incidence of developing Hyperbilirubinemia.

In the study done by Amar Taksande et al, and Rostami et al, the mode of delivery was found to be independent factor in predicting the occurrence of Neonatal Hyperbilirubinemia.[7,8]

The incidence of Neonatal hyperbilirubinemia was found to be 13.9%. The findings of our study was found to be little more when compare to other studies. In another studies done by Randev S et al, the incidence was 12%, Alpay et al, it was 12.05%, Palmer et al, it was 10.70% and Agarwal et al, it was 10.30 %.[9-12]

The presence of neonatal hyperbilirubinemia was found to be more among the subjects who had serum cord Albumin level less than 2.8. The treatment method of Phototherapy and exchange transfusion was required to the study subjects who had Serum cord albumin level less than 2.8 gm/dl. The findings of our study was found to be similar to the study findings of Sahu et al, and Trivedi et al.[13,14]

CONCLUSION

From the present study, 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 hyperbilirubinemia.

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